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CONTENTS.

	PAGE.
Bacillus Pyogenes Filiformis (nov. spec.). By Simon Flexner, M. D.,	147
A Clinical and Experimental Study of the so-called Oyster Schucker's Keratitis. By Robert L. Randolph, M. D.,	150
The Clinical Course of forty-seven Cases of Carcinoma of the Uterus subsequent to Hysterectomy. By W. W. Russell, M. D.,	154
Notes on Some Cases of Angina treated with Behring's Antitoxine. By George Blumer, M. D.,	158
Proceedings of Societies:	
Hospital Medical Society,	164
Pyarthrosis—Discussion [Dr. Halsted];—A Case of Congenital Ptosis [Dr. Thomas];—Remarks [Dr. Barker].	
Notes on New Books,	167
Books Received,	168
Notice,	168
Index to Volume VI,	168

BACILLUS PYOGENES FILIFORMIS (NOV. SPEC.).*

By Simon Flexner, M. D., *Resident Pathologist, The Johns Hopkins Hospital; Associate Professor of Pathology, Johns Hopkins University.*

[*From the Pathological Laboratory of the Johns Hopkins University and Hospital.*]

(Preliminary Communication.)

During the past winter a large healthy female rabbit of the stock of the laboratory gave birth to a litter of young, and about the fifth day following parturition, although it had not appeared ill, was found dead in its cage. Following the rule of the laboratory, which is to make autopsies upon all animals which die, this one was examined in the usual way. It is necessary to state that the young of this animal were found dead before the death of the mother occurred.

The animal bore its litter on March 13th or 14th, and was found dead on the morning of the 18th. The autopsy was performed in the afternoon of the 18th.

The body was well nourished; there was no evidence of death from violence, the mammary glands were still large, and upon section a lactiferous fluid escaped from their cut surfaces. There was no excess of fluid in the peritoneal cavity, the layers of the serosa appearing normal except as is about to be mentioned.

The condition of the uterus especially arrested attention upon the examination of the abdominal viscera. It was several times larger than the normal, although much smaller than the uterus of the rabbit at term, and presented a series of dilatations and contractions which, except for their irregular distribution, might have been mistaken for a pregnancy. This condition was, however, hardly to be considered under the circumstances, and indeed upon inspection the dilated pouches appeared thin and semi-translucent, and gave the impression of being quite empty. The serosa over the dilatations was injected; the vessels of larger size being very prominent and turgidly filled with blood, the intervening tissue presenting a rosy hue. Both cornua of the uterus were similarly affected. Nothing abnormal was observed in connection with the ovaries. On opening the uterus after its removal with the vagina attached, the pallor of the mucous membrane contrasted with the injection of the serous coat. This pallor of the mucosa was of a peculiar opaque quality and unlike the appearance of the velvety membrane itself. On gently stroking the mucosa with a knife a thick, opaque material could be removed, which appeared to be only lightly adherent to the surface of the membrane. It was to the pres-

*Read before the Johns Hopkins Hospital Medical Society, November 4, 1895.

ence of this material that the peculiar opacity was due, and the exudate extended from the vagina throughout the entire extent of the uterus. In the dilatations before mentioned the mucous membrane was of extreme tenuity, and here, as might have been expected, the layer of opaque exudate was thinner than elsewhere. The impression was given that the dilatations were brought about by accumulations of a gas. After the removal of the exudate the underlying mucosa was found to be congested. The other organs of the peritoneal cavity apparently were normal.

The pleural cavities contained fluid which was not in large amount and of a transparent hæmoglobin-red color. The serosa itself was covered with a thick shaggy layer of a fibrin-like material. Both the parietal and visceral layers were covered with this material, which was very thick over the region of the diaphragm. The lungs were in part voluminous, in part collapsed, the expanded portions being of a firm consistence and apparently consolidated. The bronchi contained fibrinous plugs.

The pericardial sac contained a small amount of fluid between layers of a shaggy appearance, due to the presence of a fibrinous-looking exudate similar to that found covering the pleuræ. It was, however, thinner here than there.

The lymph glands of the body showed no especial enlargement and the other viscera no gross pathological changes.

Bacteriological Examination. Cover-slips made from the exudate in the vagina and uterus showed a surprisingly large number of organisms which were strikingly pleomorphic. These organisms form for the most part thread-like structures; not a few, however, are much smaller. They vary from bits only a little larger than cocci to thread-like forms as long as the longest anthrax chains. At first sight there would appear to be several kinds of bacilli present; but the appearance, in both large and small forms, of a striking irregularity of staining makes this improbable. Very few of the bacilli stain regularly, for the most part brightly staining spots appearing between unstained areas. An outer membrane always stains, enclosing the stained dots in a colorless ground. A closer study reveals the stained particles to occur with much regularity, that is, they are about equidistant in the longer forms, where they are best studied, and in general they are of the same size. The threads are not as a rule straight, but present delicate sinuous and wavy outlines. The short forms are straight with rounded ends. Among these organisms a large number of pus cells and a few larger cells with single vesicular nuclei were scattered. Although many pus cells were present in the exudate, yet from the appearance of the cover-slips no inconsiderable portion of it must have been furnished by the bacilli.

Cover-slips made from the pericardial and pleural exudates, as well as from the consolidated portions of the lungs, showed the same organisms. While they were very numerous in the cover-slips from these situations, they were not as abundant as in the uterus.

Aerobic cultures were made upon various media, Loeffler's blood serum, sugar-agar, sugar-bouillon, plain agar and bouillon, the agar, urine and serum mixture; anaerobic cultures were made in plain and sugar-agar and bouillon as well as upon blood serum in Buchner's jars and an atmosphere of hydrogen. All these kept in the thermostat for several days at 37° C. showed no growth whatever.

Fearing that it would not be possible to cultivate the organism upon the usual media, the pleural cavity of a second rabbit was inoculated by breaking up a speck of the pleural exudate from the first one in bouillon and injecting the suspension with a sterilized syringe, after making a small skin incision, into this cavity. This inoculation was positive in its results.

Subsequent experiments were conducted as in the previous one by transplanting small bits of the fibrinous material from the inflamed parts of previous animals, or of the fluid which was also present in the pleural cavities in the other animals. In this way the series was kept continuous and the bacilli alive.

Considerable variations were observed according as the inoculations were made into the pleural cavity, the peritoneal cavity, the subcutaneous tissues, beneath the dura mater, or directly into the circulation.

The inoculations were positive in all cases except a few in which they were made subcutaneously. The death of the animal occurred soonest when inoculation was made beneath the dura mater. A small portion of the skull was trephined, under the usual antiseptic precautions, and a drop of the pleural fluid or a speck of the fibrinous exudate was introduced beneath this membrane, care being taken not to injure the brain. These animals, which quickly recovered from the effects of the operation, died on an average about twelve hours after the inoculation. The usual appearances were as follows: The external layer of the dura, excepting at the point of puncture, appeared quite normal; the internal layer was injected. Corresponding with the point of puncture, but smaller, a grayish-white area was visible, this being most marked in the case of the introduction of a bit of the fibrin, and doubtless consisted in part of the introduced exudate. The pia was distinctly reddened, the vessels being more prominent than normal, and the meshes of the pia contained a thin but otherwise distinctly turbid fluid. There were no pathological changes to be observed in the cortex of the brain, nor were any found in the ventricles.

Cover-slip preparations made from the point of inoculation showed, besides pus cells, a very large number of the typical bacilli. Similar preparations from the meninges at a distance from the point of inoculation also showed bacilli, but they were fewer in number, and among them more or less leucocytes with amphophilic granulations and polymorphous nuclei were scattered.

The pleural inoculations were followed by death, as before stated, in every instance, the death of the animal occurring upon the third or fourth day. The appearances presented at autopsy were for the most part an exact reproduction of those observed in the animal which had succumbed to the natural disease. Upon the side of inoculation a thick grayish-yellow shaggy membrane covered the pleural surfaces, being at times four or five millimeters in thickness. The pleural cavity contained several cubic centimeters of a clear hæmoglobin-colored fluid besides, the lung for the most part being compressed. At times smaller or larger areas of lobular pneu-

monia would be present; and as a rule the inflammation was not limited to the serous membrane of the side of inoculation, but extended into the opposite pleural cavity and into the pericardial sac. However, in these situations the process was as a rule less intense, the solid exudate being less considerable, and in the case of the opposite pleural cavity sometimes entirely wanting. The superficial vessels, however, were injected and the serous surfaces of the affected membrane covered with a slimy material. In addition to this, the opposite pleural cavity always contained a pink serum similar to that described upon the side of inoculation.

The study of the exudate upon the side of inoculation, as well as the fluid contained in the opposite pleural cavity and in the pericardium, showed the same organisms as had been introduced. They were most numerous upon the side of inoculation and in the solid portion of the exudate. So far as could be determined by the use of cover-slip preparations, they were absent from the blood and distant viscera.

The inoculation of the fluid from one of these pleural cavities into the peritoneum did not always succeed in causing the death of the animal. The periods of incubation in these cases, even when the inoculations were successful, were longer than in the previous ones, the animals affected often not dying in less than a week. The results of the peritoneal inoculations were to produce either a general sero-fibrinous peritonitis or a circumscribed fibrinous peritonitis. In several instances where the inoculations were made into the pleural cavity, an extension through the diaphragm with the productions of a localized pseudo-membranous inflammation over the liver was observed. The exudate in all these cases showed large numbers of typical bacilli upon microscopical examination.

In several instances the subcutaneous inoculation of the pleural fluid was successful. Larger and smaller areas of tissue were converted into a rigid fibrinous material in which bacilli were found in large numbers.

Perhaps the most interesting, certainly the most widespread, effects were obtained by the intravenous inoculation of the pleural fluid. The results were uniformly fatal, the animals all succumbing in from two to four days after inoculation. At autopsy abscesses were present in the viscera. These were generally miliary in size, although at times they were larger and spreading. Preferences were exhibited in reference to their localization, certain organs being entirely spared. The abscesses were never absent from the brain and heart muscle. They appeared occasionally in the liver, more rarely still in the voluntary muscles, never in the kidneys or the lungs.

The effects of the intravenous inoculations with respect to the points of localization of the bacilli were in part determined by the local conditions; for example, the inoculation into non-pregnant female animals was not followed by the reappearance of the micro-organisms in any of the structures of the genital tract, whereas in the case of pregnant animals the inoculations were followed by the re-localization of the organisms and the inflammatory process in the pregnant uterus.

The appearances first described in the uterus of the animal dead of the natural disease indicated that an accumulation of gas had occurred in this structure. This appearance was again observed in the experimental disease in this situation, and also in several instances in which the inoculations were made into the subcutaneous tissue and in the pleural cavity, in the last instance the gas bubbles appearing in the inflamed mediastinal tissues.

Cultivation Experiments. From time to time in the course of the transference of this organism from animal to animal, attempts were made to cultivate it. The repeated use of ordinary media in aerobic and anaerobic cultures failed as in the first instance. The use of more concentrated media, as for example five per cent. peptone in solid and fluid forms, also was without success. An attempt was now made to cultivate the organism upon the organs of a healthy rabbit, which were removed with all precautions and transferred to sterile test tubes. Only occasionally did one of these tubes show contamination. Those which were uncontaminated and had shown no growth for several days were inoculated with material from the experimental animals. For the first time a growth was obtained, not, however, upon all the organs. The growth was fairly vigorous upon the lungs, the heart and the uterus, and perhaps upon the kidney; no growth occurred either upon the spleen or liver. Transplantations from these growths were successful only to the extent of one or two subsequent generations. The best results were obtained by cultivating the organisms upon several one-third to one-half grown fœtuses obtained from the rabbit, upon which medium transplantations were successful through a series of six of these objects. The inoculations of animals from the sixth generation of the bacilli obtained in this way, either into the pleural cavity or into the circulation, were followed by positive results indistinguishable from those obtained by the use of the pleural fluid before mentioned.

Further facts concerning the morphology and biology of this organism, such as the question of spore formation, thermal death point, the effect of drying, the length of vitality outside the body, as well as the pathological histology of the lesions caused by it, will be given when the full details of this study are published.

THE JOHNS HOPKINS HOSPITAL BULLETIN,

Volume VII.

The BULLETIN of the Johns Hopkins Hospital enters upon its seventh volume, January 1, 1896. It will contain original communications relating to medical, surgical and gynecological topics, reports of dispensary practice, reports from the pathological, anatomical, physiologico-chemical, pharmacological and clinical laboratories, abstracts of papers read before, and of discussions in the various societies connected with the Hospital, reports of lectures and other matters of general interest in the work of the Johns Hopkins Hospital and the Johns Hopkins Medical School.

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A CLINICAL AND EXPERIMENTAL STUDY OF THE SO-CALLED OYSTER SHUCKER'S KERATITIS.*

By Robert L. Randolph, M. D.

The extent of the injury inducing the so-called oyster shucker's keratitis does not explain the violent reaction that follows. This fact seems to have impressed every ophthalmologist who has been brought into frequent contact with the disease. Cinders and small particles of steel or sand, when they lodge on the cornea, often remain in situation for several days without causing apparent infiltration of the surrounding tissue, and not infrequently does one meet with a case where a cinder has been imbedded in the cornea a considerable length of time without giving rise to anything but unpleasant subjective symptoms. The most common foreign bodies removed from the cornea are the filings or chippings of iron or copper, or particles of emery, sand and cinders. It is rare that we see an area of infiltration about the foreign body, and when this latter condition exists it usually means that the foreign substance was infected with pathogenic bacteria, or by its continued presence and consequent irritation has brought about conditions favoring the invasion and growth of micro-organisms. When we consider the remarkable resources of the eye for nullifying the effects of pathogenic bacteria we may safely say that a foreign body of the nature just mentioned, when it lodges in the cornea, will as a general rule give rise to an appreciable keratitis only after it has remained in situation for a number of days.

What is known as oyster shucker's keratitis is distinctly a traumatic affection, due to an injury from a particle of the oyster shell. The disease is chiefly remarkable for the rapidity with which an area of infiltration appears at the site of the wound, in marked contrast to the history of wounds by other kinds of foreign bodies of the same size and in the same location.

The existing evidence indicates that oyster shucker's keratitis is found more frequently in Maryland than in any other part of this country. Dr. Jas. A. Spalding, of Portland, Me., writes me that the affection is practically unknown in that part of the United States, and the same can be said of the disease in Charleston, S. C., from information kindly furnished me by Dr. Kollock of that city. The reports of the New York and Philadelphia eye hospitals contain now and then a few cases, but Baltimore seems to carry off the palm. In New Orleans the disease as such appears to be unknown. The reports of the eye hospitals in Baltimore contain the records of several hundred cases during the past few years.† The frequency of the disease in Maryland may be explained by the fact that the oyster industry is a more extensive one in that state than it is anywhere else in the world. Cases of the disease do occur no doubt in New Orleans and Portland, Me., so that probably latitude has nothing to do with determining its existence, nor is there any reason for supposing that the keratitis is to be traced to some organic or inorganic property peculiar to the oyster shell of the Chesapeake Bay.

Baltimore is the greatest oyster market in this country, and, according to Ingersoll ("The Oyster Industry," by Ernest Ingersoll, Tenth Census of the United States, Washington, 1881), there are at least six thousand shuckers in Maryland, and most of these are found in the shucking houses of Baltimore. In many of the northern cities, as for instance in Portland, Boston and New York, oysters are received in great quantities that have been shucked in Baltimore, so that oyster shucking in those cities evidently does not exist as a trade to the extent that it does in Baltimore. The magnitude, then, of the oyster industry in this city may be said to account for the frequency of oyster shucker's keratitis.

In a large number of the cases reported here the oyster shuckers had been plying their trade for many years and had been struck for the first time. In two cases the men had shucked for eighteen years without being struck, and it is surprising to note the fact that in none of the sixty-five cases reported were there any novices (new hands). It will be seen then that it is possible to shuck oysters for many years and still to escape injury from a particle of shell, and that the great majority of oyster shuckers escape altogether. Hence we cannot regard the disease as a very common one. It is more than probable that long familiarity with the work breeds contempt of its dangers, and this may explain why in nearly all cases it is the veteran who is wounded and not the recruit. It is very much the same kind of danger that surrounds the mechanic at the emery-wheel. Possibly the danger is a little greater in the case of the oyster shucker. Considering then the number of oyster shuckers in Maryland and the quantity of work done, it may be said that the disease is of exceptional occurrence.

Causes: As I have said, the disease is distinctly of traumatic origin; that is, a minute particle of the oyster shell is violently chipped off by the hammer* that is used in the shucking process, and it flies into the eye. The particle is generally too small and too light to penetrate to any distance into the cornea. Large pieces, however, are sometimes detached and are driven through the entire thickness of the cornea, and when such a thing happens loss of the eye usually results. This occurrence is happily rare. Unlike other foreign bodies that lodge in the cornea, the particle of shell can seldom be detected. This I think is due to the fact that in the rapid infiltration that takes place the particle of shell is thrown off. It is no

* Read before the thirty-first annual meeting of the American Ophthalmological Society, in New London, Conn., July 17 and 18, 1895.

† I have been informed by one of the staff of the Presbyterian Eye and Ear Hospital that during the past three months twenty-four cases have been treated at that hospital.

* The use of the hammer to break off the edge of the shell before introducing the knife-blade constitutes the chief element of danger in oyster shucking as practiced here in Maryland. In other sections, as for instance in the far South and down East, the shucker dispenses with the hammer and sticks in the point of the knife at once in order to pry open the shell. This no doubt explains why the disease is seldom seen in the portions of the country just mentioned.

uncommon thing to see a particle of steel that is surrounded by a necrotic area drop out at the slightest touch, and sometimes we meet with these small points of infiltration where no foreign body can be detected, it evidently having been dislodged or thrown off in the suppurative process. In two or three instances I have succeeded in removing from the centre of one of these areas of infiltration a small particle of what was undoubtedly a piece of shell. My friend, Dr. B. W. Goldsborough, who lives in Cambridge, Md., one of the smaller oyster shucking centres, tells me that he has more than once removed small particles of shell from these infiltrated areas. No doubt in many cases the piece of shell simply strikes and wounds the cornea without lodging in it. The superficial nature of the injury readily explains why the particle of shell would be apt to drop out as soon as infiltration began.

Symptoms: The photophobia in oyster shucker's keratitis is marked. The patient tells us that he has a defined sensation of having been struck in the eye. This sensation is not usually followed by pain until some hours later. Frequently the exposure to artificial light, as for instance the lighting of the gas or lamp the evening of the same day, will mark the time when the unpleasant symptoms begin. From now on the pain is usually intense, and the clinical symptoms resemble those of phlyctenular keratitis somewhat intensified.

In an article which appeared in the *Virginia Medical Monthly* about fifteen years ago*—which article, by the way, is the only publication known to me on this subject—the writer states that the position of the ulcer is a constant one, that it is always found in one place, and this is the centre of the cornea. The most exposed part of the cornea is the point that is usually struck, and as this part represents an area through which the visual line is passing at the time, and as the visual line always passes through the cornea somewhere near the centre, the location of the wound will be here, and for no other reason, though this explanation does not seem to have occurred to the writer of the article referred to, other reasons being given by that writer for the location of the keratitis. It may be added that this location of the ulcer is not an invariable one, for I have frequently noticed a peripheral situation.

There is usually more or less circumcorneal hyperæmia. The ulcer is very white, whiter than other corneal ulcers. I have never seen such an ulcer with blood-vessels running to it, and its size no doubt is dependent more or less upon the size of the particle of shell. The ulcer is sharply circumscribed as to its borders, which, instead of fading off gradually into the adjacent tissue, will be seen to lie adjacent to perfectly transparent cornea. Such an ulcer suggests more strongly a chemical than a parasitic origin. The ulcer does not show the same tendency to spread as do other corneal ulcers, and when the keratitis assumes a diffuse character it is probably an evidence that bacteria have invaded the tissue at this point. Such complications do occur. I have seen such an ulcer remain absolutely localized for two or three weeks without any apparent departure from its original borders. On this account the prognosis is favorable, though this is largely governed by the size and depth of the wound. A perforating wound of the cornea or a wound involving a large area is usually followed by loss of the eye, and this is especially true when the former condition is present.

Treatment: The yellow salve has proved useless in our hands. The galvano-cautery was used in a certain number of cases, but it did not seem to exercise any specific influence for good, and the same can be said of eserine. A compress bandage and a mild sublimate solution ($\frac{1}{4000}$) used every four hours, together with an occasional drop of a solution of atropia —1 per cent.—have given the best results. To this treatment the keratitis responds promptly, and in a week or ten days the subjective phenomena have been so ameliorated that the shucker can resume work. The opacity can be detected by oblique illumination and is permanent. In several cases where the shuckers had been struck more than once, I found the old nebulæ.

The striking point in these cases is the rapidity with which an area of infiltration makes its appearance at the site of the injury. These areas range in size from a pin's head to twice these dimensions, and even larger. The condition differs so entirely from what we are accustomed to see from injuries caused by other kinds of minute foreign bodies that it has occurred to me that the oyster shucker's keratitis might be due to some specific micro-organism. With this idea in view, I made microscopical examinations and inoculations on culture media, using chiefly nutrient agar, from sixty-five cases of oyster shucker's keratitis, of which the following fifteen cases may be taken as a fair sample of what the bacteriological examinations disclosed. In making inoculations a sterilized dropper and cocain solution were used for anæsthetizing the cornea. The point of the platinum needle was well forced into the necrosed tissue, and in nearly all cases small particles of the wall of the ulcer were brought away and carried into the agar tube. In every case Esmarch tubes were made, which were promptly placed in the thermostat.

F. H., struck in left eye three days ago. Central ulcer. Pain and photophobia intense. There was nothing definite in the cover-slips, and after twenty-four hours there was no growth on the agar.

J. R., struck in right eye with particle of shell yesterday. Large ulcer and marked area of infiltration. Eye very painful. Inoculations into three agar tubes. Two cover-slips were made, and one stained with methylene blue and the other with gentian violet. In both cover-slips small micrococci were to be seen, occurring as diplococci. In tube *A* there was a diffuse growth, and at some points the colonies looked round and flat, and an examination of several of the colonies showed the same organism, a short bacillus. There was no growth in tube *B* (inoculated from *A*). In a third tube where the inoculation was made directly from the ulcer there was an abundant growth of what was evidently an impurity.

J. H., struck in left eye three weeks ago. At the present time there is a violent kerato-iritis; the pupil being contracted and pus in anterior chamber. Two ulcers on the cornea. Cover-slips from the ulcer showed nothing. In tube *A* there was a round, large and slightly iridescent colony with reddish centre and yellow halo, which was the only colony in this tube. This turned out to be an enormous micrococcus. In tube *B* the agar was dotted with a fine growth, the colonies being very numerous and revealing under

*Oyster Shucker's Corneitis, by W. J. McDowell, M. D., Va. Med. Month., Vol. V, page 883.

the microscope bacilli of at least three varieties. The inoculations were made into both tubes directly from the ulcer.

P. S., large ulcer in centre of left cornea from an injury received yesterday. Cover-slips showed nothing definite. In tube *A* there was a vigorous growth of several varieties of bacteria. In tube *B* (inoculated from *A*) there were two kinds of bacilli, one staining very deeply and having rounded ends, and the other bacillus being more slender and having sharply cut ends. Both these bacilli were present in tube *A*. Tube *C* contained nothing.

A. G., struck in left eye yesterday. Small central ulcer. Cover-slips negative. In tube *A* after twenty-four hours there was a small round white colony that turned out to be the staphylococcus pyogenes albus. There was no growth in tubes *B* and *C* (representing the first and second dilutions of tube *A*).

W. H. W., struck in left eye yesterday. Minute ulcer on the nasal side of the centre of the cornea. Cover-slips showed nothing. Tubes *A* and *B* contained numbers of small white colonies scattered over the surface of the agar, and examination showed them to be bacteria of various kinds and shapes. (*B* was inoculated from *A*.) Tube *C* was inoculated direct from the eye and contained two colonies of a long slender bacillus.

R. L., left eye, small central ulcer. Was struck yesterday. Cover-slips vague. Tube *B* inoculated from *A* contained a bacillus and large micrococcus. Tube *C* contained nothing.

T. W., struck yesterday. Central ulcer. Pain intense. Struck for the first time, though he has shucked oysters for fifteen years. Cover-slips and cultures negative.

C. L., struck in right eye yesterday. Large ulcer somewhat below the equator of the cornea. The staphylococcus aureus was found in this case.

G. J., struck in left eye six days ago. Small ulcer on periphery of the cornea. On the second day tube *A* was found to be dotted with small white colonies which turned out to be a short bacillus. This bacillus was also found in tube *B*. Nothing grew in tube *C*.

G. B., struck two days ago, and pain did not come on till he went home that evening and faced the lighted lamps in his house. The staphylococcus aureus and two varieties of bacilli were found in the agar, one a short heavy bacillus and the other a short slender bacillus.

J. B., struck three days ago in the left eye. Small central ulcer. Small colonies of two kinds of bacteria in tube *B* (inoculated from *A*). One of these was the staphylococcus aureus and the other was a large bacillus.

A. S., struck in right eye three days ago. Small ulcer nearly central. Struck in same eye a year ago. Has been shucking for eighteen years. Cover-slips vague, but in tube *C* there grew the staphylococcus albus and a bacillus. Three tubes made, tube *C* being second dilution of tube *A*.

F. R., struck three days ago in the left eye. Central ulcer. There was nothing on the cover-slips, and in both tubes *A* and *B* there was a large stumpy bacillus. *B* was inoculated from *A*.

W. J., struck in right eye yesterday. Large central ulcer. One of the cover-slips showed a large micrococcus that also was found in tube *B*. This tube was inoculated from *A*.

In eleven cases out of the sixty-five there was absolutely no growth on the agar. This is not surprising when we consider the very small surface or area from which the inoculations were made. I took particular care never to touch any part of the cornea but the ulcer, and as this always occupies a very prominent position on the cornea it is likely that most bacteria would be swept off into the conjunctival sac by the constant movements of the lids. In thirty-nine cases the bacteria were of various kinds, and there were no two cases presenting the same bacteriological conditions. As a rule bacilli were the predominating organisms, and usually they were large and coarse. In three of the fifteen cases given in full I found the same bacillus, about the size of the bacillus subtilis, possibly somewhat shorter. I made a suspension of this organism in sterilized water and injected a few drops into the cornea and conjunctiva of a rabbit's eye, but scarcely any reaction followed. In several of the cases where there appeared to be some similarity between the organisms I tried the effect of injecting a suspension of the organism into the cornea, but always with negative results. In five cases the staphylococcus pyogenes aureus or albus was found. The injection of a suspension of this organism into the cornea was followed by suppuration, a thing, of course, to be expected. Inasmuch as the pyogenic staphylococci are found in several other external diseases of the eye, and even in the normal conjunctival cul-de-sac, to say nothing of their association with inflammation in other parts of the body, and moreover the fact that they were found in only five cases out of sixty-five, we are justified in the conclusion that the pus organisms had nothing specifically to do with the inflammation in those cases where they were discovered.

Were oyster shucker's keratitis a parasitic disease, certainly its specific organism, if recognizable by our present means of investigation, would have been found in several of the cases; but, as I have said, in only three cases did I find the same organism present, and the experiments with this organism seemed to show that it was possessed of slight, if any, pathogenic properties. It may be added that being once struck did not produce immunity, as there were several shuckers among the sixty-five who had been wounded twice in the same eye.

Is the disease of chemical origin? is there any chemical substance in the juice or shell that produces this immediate and intense reaction in the human cornea? To test this hypothesis I obtained about an ounce of the oyster juice, to which I added about a teaspoonful of the chippings from the shell and then passed this mixture through a Pasteur filter. I always made the oyster shucker open the oyster into a vessel so that I could obtain the juice fresh. This fluid after being filtered was injected from a sterilized hypodermic syringe into the cornea and conjunctiva of a rabbit's eye. Fifteen experiments of this character were made and the result in every case was negative, a fact that goes to show that in so far as the rabbit's cornea is concerned the juice of the oyster manifests no pathogenic effect when injected into that part of the eye.* In the first case I obtained a beautiful kerato-iritis in one eye, and in the other eye an ulcer not unlike the ulcer produced by the oyster shell. On examining the filtrate I found that it contained two varieties of bacteria—in other words, that it was infected. The injection, though, of these bacteria (both were bacilli) into the cornea of the rabbit was in no instance followed by a keratitis, so that the inflammation in the first case must have been due to some organism not found in the oyster. In the other fourteen cases I obtained a filtrate free from micro-organisms, and this filtrate was shown to possess no pathogenic properties when injected into the cornea of a rabbit.

* It may be well to state that in only one or two series of experiments did I use the same filtrate. Fresh juice was obtained and filtered for every experiment.

The bacteriological study of these cases would seem to indicate that the so-called oyster shucker's keratitis is not of parasitic origin. A number of experiments with the oyster juice after the latter has been freed of its living organisms goes to show that the juice of the oyster probably has nothing to do with the causation of the keratitis seen among oyster shuckers, and furthermore that the injection of this juice, even as much as a syringeful, under the skin of a rabbit was in no case followed by inflammation. Nor when the unfiltered juice was injected into the cornea was it followed by any irritating effect. It remained to be seen whether there was any chemical ingredient in the shell capable of calling forth this inflammation.

Several fresh oysters were procured and the edges were chipped off and ground up fine. The edge of the shell was selected, as it is this part that is chipped off by the shucker. These particles were then sterilized in a test tube. The heat did not seem to alter the size of the particles. The reaction of this substance was decidedly alkaline. I made a very small wound in the cornea of a rabbit with a cataract knife and rubbed in gently with a platinum needle a few particles of the powder. This experiment was performed eighteen times and in every case I succeeded in getting a well defined ulcer. The ulcer was accompanied with little or no circumcorneal injection, and its edges were sharply cut and separated from the healthy cornea. These experiments show beyond a doubt that there is something in the oyster shell that when introduced into the cornea will produce keratitis.

It is difficult to imitate successfully all the conditions connected with a foreign body in the cornea. In the first place, the size of the foreign body is problematical, and the most difficult thing to imitate is the manner and force with which it strikes the cornea. I thought that it would be possible to approach this latter condition by using what the boys call a blow-gun or spit-blower. It was seldom that I succeeded in blowing the particles of shell with force sufficient to drive them into the cornea. Twelve experiments of the following character were performed. One long blower was loaded with cinders from a locomotive smoke-box, and another blower was loaded with particles of oyster shells. Both the cinders and shells were sterilized. At a distance of six inches from the cornea the load was blown into the latter. In a few cases a cinder remained sticking in the cornea, but in only one case did a particle of shell stick; the particles of shell were too fine to be blown with force sufficient to make them lodge on the cornea. It was noticeable, though, that the reaction was more or less intense in the eye into which the shells had been blown, while there was practically no reaction in the eyes into which the cinders had been blown. In the case of the eyes where the shell was used, redness of the conjunctiva and increased secretion were seen, while in the other class of cases the conjunctiva remained normal. The reason that I failed to get an ulcer was that I never succeeded in wounding the cornea to any extent.

It could hardly be expected that the reaction in the case of a rabbit's cornea would be as intense as that following similar injuries in man. I have always been impressed with the promptness with which injuries to the eyes of dogs and rabbits heal. Injuries that, in the case of human beings, necessitate long and careful treatment, get well readily in rabbits and dogs. Spontaneous affections of the rabbit's conjunctiva are comparatively rare. This is not the case to the same extent with dogs, which, like man, are not infrequently seen with eye affections. The tissues, too, of a rabbit's eye are certainly more resistant to infected wounds than those of man. This fact I have demonstrated elsewhere again and again. It is not likely then that we would get a keratitis in a rabbit that resembled exactly what we are accustomed to see in the oyster shucker. The keratitis in the shucker would be more intense in its clinical history, simply because it is the human cornea that is affected; this intensity being due perhaps to the frequent presence in the conjunctival sac of pathogenic bacteria, and to the feebler resisting powers of the tissues.

It is reasonable to suppose then that any agent that will produce an ulcer in a rabbit's cornea will certainly have the same effect on the human cornea. It has been shown that, with the exception of the pus organisms, none of the organisms found in the sixty-five cases of oyster shucker's keratitis produced keratitis when injected into the cornea, that is to say, there was no apparent infiltration of the cornea at the point of injection; and this, added to the fact that no one organism was found constantly present, inclines one to the opinion that the disease is probably not of bacterial origin—this in the light of our present bacteriological knowledge. It has been shown that the oyster shell contains an inorganic material that does produce keratitis when introduced into the corneal tissue.

The analysis of Chatin and Muntz* shows that the shell of the oyster contains considerably over 90 per cent. of calcium carbonate. The analyses show that carbonic acid held in combination with calcium and magnesium is present to the extent of 44 to 48 per cent., and that calcium oxide varies from 49 to 53.7 per cent., and magnesium oxide from 0.4 to 0.5 per cent. The tables further show that sulphates, phosphates, silicates, fluorides, bromides and iodides are present, the sulphates forming about 1½ per cent., the phosphates $\frac{1}{10}$ per cent. and less, the silicates 2 to 3 per cent. and more, the fluorides a few hundredths of 1 per cent., the bromides and iodides some thousandths only of 1 per cent. The bases corresponding are calcium, magnesium, iron and manganese. Organic matter is present to the extent of 1 per cent., and remains in the form of a thin membrane or network when the mineral matters are dissolved out of the shell with the help of acids. It will be seen then that the carbonate of lime forms nearly all of the oyster shell.

I obtained some pure carbonate of lime (not the chalk such as is furnished by the druggist), and after making a sterilized wound of the cornea, powdered some of the lime that had been previously sterilized, between the lips of the wound, and in every instance I succeeded in getting an appreciable keratitis. This experiment was repeated with positive results a number of times. It would seem then that the carbonate of lime is in itself sufficiently irritating to call forth an inflammation of the cornea under certain conditions.

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*Analyse des coquilles d'Huitres, par MM. A. Chatin et A. Muntz, Comptes Rendus, t. CXX, 53.

In this connection it is interesting to note the fact that on the Eastern Shore of Maryland, in the latter part of September and during October, when the winds are very high and the roads dusty, a form of ophthalmia is very common, which is attributed to the fine particles of oyster shell dust that fill the air and get into the eyes of those who drive along the roads. The roads in that section are for the most part shell roads. The ophthalmia is characterized by great redness of the conjunctiva and profuse secretion. Not infrequently both eyes are affected, and it is a very painful affection. I am indebted to Dr. B. W. Goldsborough of Cambridge for information on the subject of this interesting eye disease, which he tells me is often seen in his section of the country at certain seasons. This certainly shows that the oyster shell possesses irritating qualities. Accounts are contradictory as to the irritating effect of the dust on a well-known shell road in the vicinity of Baltimore.

It has been suggested that the mud which covers the oyster probably flies into the eye and causes the trouble. Any one who has visited an oyster shucking establishment will be struck at once with the appearance of the shuckers. Their hats, faces and the upper portions of the body are peppered with fine particles of mud, and I have been told over and over again that the mud frequently flies into the eyes, but other than a little temporary burning no inconvenience follows. The face is often the seat of hundreds of little points where a drop of mud has struck and hardened. I am sure that were the injury inflicted in this manner we would meet with the disease far oftener, in fact oyster shucker's keratitis would be a very common affection, but it has been shown that the disease is of exceptional occurrence.

As to any other ingredient of the oyster shell playing a role in the production of the keratitis I am unable to give any evidence at this time. Positive evidence exists to show that the carbonate of lime possesses properties irritating enough to produce keratitis in the cornea of rabbits and dogs, a keratitis of a sluggish character. And though no typical picture of oyster shucker's keratitis was obtained in these animals, it is highly probable that the peculiar aspect of the disease as seen in man is due to conditions belonging to the human eye alone, conditions which help to intensify the process. It is more than likely that some one or more of the other chemical ingredients of the shell may play a part in the etiology of the keratitis. From the analysis of Chatin and Muntz it is evident that the oyster shell contains ingredients besides the carbonate of lime which might be irritating to the cornea and conjunctiva.

Conclusions.

1. Oyster shucker's keratitis may be defined as a traumatic keratitis where the injury is produced by a particle of the oyster shell.

2. The disease is chiefly remarkable for the rapidity with which the cornea undergoes necrosis at the site of the injury, this area of necrosis being usually very small, owing no doubt to the small size of the foreign body. Small foreign bodies of copper, steel and sand usually produce no appreciable keratitis; and even when they lodge in the cornea, commonly require several days to cause a noticeable inflammation. On the other hand, the oyster shucker presents a marked infiltration of the cornea at the point of injury within twenty-four hours after the accident.

3. This decided reaction on the part of the cornea makes the injury a peculiarly dangerous one when a large area is wounded, or when entrance has been made into the anterior chamber, such conditions in my experience being invariably followed by loss of the eye through panophthalmitis. How often do we see the cornea injured in the same degree by other kinds of foreign bodies and still the vision not entirely destroyed.

4. Bacteriological investigations failed to discover any specific organism, nor did any of the organisms obtained from cases of oyster shucker's keratitis manifest any pathogenic properties when introduced into the corneæ of rabbits, with the exception of the pyogenic cocci. It is not likely then that the disease is of parasitic origin.

5. The carbonate of lime, of which the oyster shell is almost entirely composed, was found to possess qualities irritating enough to call forth a keratitis when introduced into the cornea of a rabbit, and it is more than probable that several other chemical ingredients of the shell would be more or less irritating to the cornea.

6. It is certain that bacteria always play a part in traumatic keratitis, but it is evident that in this variety of traumatic keratitis the cornea is rendered especially susceptible to the effects of micro-organisms, by the irritating chemical ingredients of the oyster shell, notably the carbonate of lime.

THE CLINICAL COURSE OF FORTY-SEVEN CASES OF CARCINOMA OF THE UTERUS SUBSEQUENT TO HYSTERECTOMY.

By W. W. Russell, M. D., *Associate in Gynecology.*

(*Read before the Johns Hopkins Medical Society, November* 4, 1895.)

The doubts which have existed as to the ultimate value of complete extirpation of the uterus for carcinomatous growths can be set aside with certainty. From the statistical reports of many operators we are now justified in claiming the possibility of cure in a certain number of cases by removal of the uterus, or a relief from distressing symptoms for months and even years. We obtain then by such a procedure either a cure or a palliative effect, very often anticipating a cure where we obtain only cessation for a variable period of the local discharges, hemorrhages and pain.

It is commonly accepted that these patients live usually not over two years after the appearance of the first local signs.

If we are able then to free them from this terrible affliction for a longer time than this, even though recurrence does result in the end, are we not justified in the procedure? The indication for operation is to obtain a cure, although ultimately there may be only temporary relief.

Our results clearly illustrate this fact, as sixteen of the twenty-one cases still living have passed the limit of two years and are enjoying good health—a period of exemption well worth the trial.

The following forty-seven cases of hysterectomy for carcinoma of the uterus include all those operated upon by Dr. Kelly and myself since the opening of the Gynecological wards in October, 1889, and in Dr. Kelly's private practice up to October, 1895, thus giving a time limit of from one to five years.

Many of these cases we have seen personally within the past three months, and where they lived at a distance we have obtained our information by writing to the local consultant or to the patients themselves.

Vaginal hysterectomy has been employed in forty cases, abdominal in four, and the combined operation in three cases.

Grouping them all under one head the results are as follows:

Death from primary effect of operation.....	5 = 10	per cent.
Patients still living	21 = 44	"
Patients died with recurrence	16 = 34	"
Patients not heard from	4 = 8	"
Died from heart lesion.....	1 = 2	"

Three of the deaths immediately following the operation were due to peritonitis and two to ligation of the ureters.

Recurrence and death took place in the sixteen cases within eighteen months, but the prognosis in eight of these at the time of operation was unfavorable.

One patient of the twenty-one still living was operated upon nearly five years ago for extensive disease springing from the cervix. She presented herself in perfect health about every six months for examination, but we were never able to find any return of the trouble locally. About sixteen months ago there appeared in the left side of the neck above the clavicle a nodule, to which she called our attention. Since then other glands in this region, on the opposite side of the neck and in the axillæ, have become similarly affected, some of which have broken down and discharged externally. She is at present in a critical condition. As her home is at a considerable distance, we are compelled to accept this as a metastatic manifestation.

Two cases died within four months after the uterus was removed. One had at time of operation such extensive infiltration on either side of the cervix that the case was considered hopeless. The uterus in the second case was found during the operation converted into a friable carcinomatous mass adherent in every direction to the bowels, so that complete enucleation was impossible.

Carcinoma of the breast developed and was removed in two cases several months after the uterus was extirpated. One of these died of a pre-existing heart lesion without any evidence of a local return, and the other is at present also free from any pelvic trouble, but the carcinoma has again appeared in the breast.

The Fallopian tube prolapsed in three cases in which it had not been removed, and during the healing of the vaginal incision was caught so that it protruded into the vagina, greatly reddened and swollen. These upon examination made us suspicious that there had been a return of the disease, but the microscope proved their true character. Two of these patients are still in good health; the third died from a recurrence.

Another patient returned a year after operation with a note from her physician telling me that he had discovered a mass in the vaginal vault which he believed to be of a malignant character. There had been associated with it a profuse vaginal discharge, and occasionally some bleeding. This mass proved to be a large silk ligature which had been left on the broad ligament and had become imbedded in the granulation tissue. Since the removal of the ligature the patient has been absolutely well.

The most interesting of these cases is a patient who presented herself three months after vaginal hysterectomy for carcinoma of the cervix, with a fungus-like growth arising in the vaginal vault along the scar resulting from the operation. Dr. Kelly dissected the mass carefully out and thoroughly cauterized the surrounding area. This took place two and a half years ago, and the patient at present continues to be in excellent health.

Local return occurred in all the cases terminating fatally, but in none could we elicit any history of metastatic growths in other parts of the body, the single exception being the one case above cited where the patient is still living.

Pneumonia was the cause of death in one instance thirteen months after the operation; here there was an extensive malignant ulcerated area in the vaginal vault, which had appeared a few months after she left our care.

Adeno-carcinoma, body of the uterus	9 cases.
Carcinoma, cervix.....	38 "

Results of hysterectomy for carcinoma of the body:

Patients still living	7 = 77	per cent.
" died recurrence, operation incomplete.....	1 = 11	"
" died primary effect of operation.....	1 = 11	"
No. cases still living, 5 yrs. elapsed	1	
" " " 3 " "	2	
" " " 2 " "	2	
" " " 1 " "	2	

The uterus was removed by supravaginal amputation in three cases. An ordinary vaginal hysterectomy was performed in the remaining six. Recurrence has taken place therefore only in the case where the operation was not completed.

In some of the cases the growth had penetrated the walls of the uterus so that it could be seen just beneath the peritoneal covering, and yet no evidence of involvement of the lymphatics or the parametrium could be detected. The three cases in which the cervix was left have proved as satisfactory as those in which the whole uterus was removed.

Results in hysterectomy for carcinoma of the cervix:

Patients died from primary effect of the operation	4 = 10	per cent.
Patients still living	14 = 36	"
Patients died with recurrence	15 = 38	"
Patients not heard from	4 = 10	"
Operations over 4 years ago and patients still living	3	
" 3 " " "	4	
" 2 " " "	4	
" 1 " " "	3	

The uterus was removed in four cases by the combined method. One of these died a few days after the operation from ligation of the ureter, and another in which the disease was associated with pregnancy died several months after operation with a recurrence in the vagina. The remaining two are reported as free from any suspicious signs.

Vaginal hysterectomy was employed in thirty-four cases, three of which died from the operation, and fourteen afterwards from the original disease.

The four cases not accounted for up to the present time were considered at the time of operation favorable for cure. Two of them I have since seen, one two years after operation and the other one year, and both at that time showed no evidence of ulceration or induration by vaginal examination.

The fourteen women who are still living do not give symptoms pointing to metastasis or local recurrence, except the one mentioned with the nodules in the neck and axillæ. This single case proves that even after a lapse of four years we are not justified in claiming a cure. We cannot definitely at present fix a period of years through which a patient must live in order to pass the danger limit. Fritsch, Schauta, Hofmeier, Leopold and Boldt have followed their cases from five to seven years after the removal of the uterus, and even as late as seven years there continues to be a fall in the percent. of cures.

Olshausen, Schauta and Fritsch report over 47 per cent. without recurrence after a lapse of two years. It is a striking fact that in our cases thus far, all recurrences but one have taken place within eighteen months.*

We have not attempted to show the relationship of the different forms of carcinoma to their tendency to recurrence, but the form of disease has undoubtedly a great influence upon the ultimate results. This point is clearly demonstrated by our experience, as in not a single one of the seven cases in which the uterus was completely removed for adeno-carcinoma of the body has a recurrence been noted; while in the thirty-eight cases where the cervix was diseased, fifteen have died with a return of the trouble.†

Metastases were found only once beyond the pelvic and retroperitoneal glands, in ten autopsies performed in the pathological laboratory upon patients in whom carcinoma of the uterus was present. This was an adeno-carcinoma of the body of the uterus, and a few nodules were found in the liver. In four others there were carcinomatous deposits in the pelvic and retroperitoneal glands.

This, in conjunction with the fact that by far the greater majority die subsequent to hysterectomy with a continuation of the growth in the vagina and parametrium, proves the possibility of complete eradication.

*Statistics obtained from Winter, Berliner klin. Wochenschrift, 1891, No. 33, and Ztsch. f. Geburtsh. u. Gyn., Vol. XXIV, p. 135; also Boldt, American Jour. Obstet., Vol. 26, p. 517.

†Kinkenburg (Ztsch. f. Geburtsh. u. Gyn., Vol. 23) and Hofmeier (same journal, Vol. 32) have made similar observations.

STATISTICS OF FORTY-SEVEN CASES OF CARCINOMA.

NAME.	SEAT OF DISEASE.	OPERATION.	DATE OF OPERATION.	DATE OF DEATH.	REMOTE RESULTS.
Mrs. L.	Cervix. Fungating mass filling upper portion of vagina.	Vaginal hysterectomy.	11-21-89	8-30-91	Local return.
E. C.	Body.	Vaginal hysterectomy. Uterus ruptured during removal.	1-2-90		Patient continues to be in excellent health.
C. G.	Cervix. Previous operation, high amputation.	Vaginal hysterectomy. First use of ureteral catheter.	6-18-90		Patient last examined 10-2-92. No sign of return.
D. J. B.	Body.	Vaginal hysterectomy. Bladder opened.	8-28-90	Five days after operation.	Death, peritonitis.
Mrs. H.	Cervix. Extensive lateral infiltration.	Vaginal hysterectomy.	3-28-91	Five months after operation.	Local return in vaginal vault.
M. W.	Cervix. Fungating mass in vagina.	Vaginal hysterectomy.	4-4-91		Last examination 10-2-95. No evidence of return.
J. B.	Portio vag. Disease extends 1 cm. on vaginal walls.	Vaginal hysterectomy.	5-4-91		Discharging glands in neck and axillæ. No local return, 8-15-95.
E. C.	Cervix. Disease circumscribed.	Vaginal hysterectomy.	7-1-91		Last seen 8-9-93. In perfect condition.
M. A. B.	Cervix. Fungating mass in vagina. Extensive lateral involvement.	Vaginal hysterectomy.	11-9-91	9-5-92	Local return in few months.
Dr. Miller's Patient.	Cervix.	Vaginal hysterectomy.	4-22-91		Excellent health. No evidence of return, 9-11-95.
Mrs. W.	Cervix. Lateral involvement. Myoma at fundus.	Vaginal hysterectomy.	12-23-91	1-1-93	Local return.
K. K.	Cervix. Extensive lateral infiltration.	Vaginal and abdominal.	1-30-92	Died from operation. Ligation of ureters.	
Mrs. M.	Cervix.	Vaginal hysterectomy. Cauterization of left pedicle on account of infiltrated area. Prognosis bad.	2-18-92		Patient in excellent health. No local return, 9-15-95.

NAME.	SEAT OF DISEASE.	OPERATION.	DATE OF OPERATION.	DATE OF DEATH.	REMOTE RESULTS.
Miss B.	Body.	Incomplete vaginal hysterectomy on account of extensive disease and infiltration of fundus.	2-23-92	About three months after operation.	Disease had broken through uterine wall and spread out on intestines.
Mrs. G.	Cervix.	Vaginal hysterectomy.	8-3-92		9-28-92. Portion of tube in incision removed with cautery. 9-1-95, patient in good health.
F. C.	Cervix. Two nodules found in uterus entirely separate from cervix.	Vaginal hysterectomy. Bladder perforated and afterwards closed with good result. Bad prognosis.	11-27-92	10-18-93	12-12-95. Prolapsed tube excised. Local return.
C. T.	Cervix. Complicated by 4 months' pregnancy.	Vaginal and abdominal.	11-10-92	5-1-94	Patient died in Hospital. Local return with perforation of bladder and rectum.
R. A.	Body. Associated with myoma.	Supra-vaginal amputation. Cervical canal cauterized.	11-28-92		Patient in good health, 9-13-95.
Z M. S.	Cervix. Fungating mass in vagina.	Vaginal hysterectomy.	12-17-92		5-13-93. Ulcerated area in vaginal vault dissected out and cauterized.—9-31-95. No sign of local return.
A. E.	Cervix. Fungating mass filling vagina. Invasion of vaginal mucosa.	Vaginal hysterectomy.	6-25-93		Unable to find patient.
Mrs. D.	Cervix.	Vaginal hysterectomy.	3-6-93		Patient continues in good health, 10-1-95.
Mrs. C.	Cervix.	Vaginal hysterectomy.	4-12-93		Unable to obtain information regarding patient.
Mrs. G.	Cervix.	Vaginal hysterectomy. Impossible to remove all disease laterally.	4-18-93	7-1-93	Local return.
E. B.	Body.	Vaginal hysterectomy. Uterus ruptured in removing.	5-10-93		Breast removed for cancer about one year after hysterectomy. 10-1-95, no return in vagina, but patient under treatment for some recurrence in breast.
Mrs. S.	Cervix.	Vaginal hysterectomy.	8-30-93	Died one year later.	Local return.
S. L.	Cervix. Vagina filled with fungating mass, and infiltration for 2 cm. about cervix.	Vaginal hysterectomy. Bladder perforated. Transfusion of salt solution in radial artery.	10-10-93	8-15-94	Local return.
P. H.	Cervix. Circumscribed nodule.	Vaginal hysterectomy.	11-8-93		Last heard from 8-20-95. Doubtful return in cicatrix.
L. W.	Body. Associated with myoma.	Supra-vaginal amputation.	2-15-93		Continues in excellent health, 10-5-95.
C. S.	Cervix.	Vaginal hysterectomy.	11-25-93	Died from operation. Peritonitis.	
M. F. W.	Portio vaginalis. Disseminated nodules in vaginal mucosa.	Vaginal hysterectomy. Whole upper third of vaginal mucosa removed.	11-25-93	2-1-95	Death from pneumonia. Local return.
M. G.	Body.	Vaginal hysterectomy.	12-4-93		Continues to be in excellent health, 8-17-95.
M. D.	Cervix. Lateral infiltration so far advanced that a bad prognosis given.	Vaginal hysterectomy. Bougie in ureter.	12-11-93		No evidence of local return. Patient in excellent health, 9-13-95.
A. R.	Cervix. Post. lip only involved.	Vaginal hysterectomy.	1-31-94		Sent by physician for examination on account of suspicious nodule in scar, which proved to be silk ligature imbedded in granulation tissue. No evidence of return of disease, 9-13-95.
L W.	Cervix. Fungating mass filling upper portion of vagina. Mucosa of vagina not diseased.	Vaginal hysterectomy. Bougie passed into ureter.	2-15-94	About nine months after operation.	Local return.
N. C. J.	Cervix. Uterus torn off above internal os. Lateral infiltration. Bad prognosis.	Vaginal hysterectomy.	2-17-94	6-3-94	Local return.
E. O.	Cervix. Lips entirely disappeared. Disease far advanced laterally.	Vaginal hysterectomy. Uterus ruptured during removal.	3-3-94	11-5-94	Local return.
S. B. H.	Cervix. Nodules felt beneath vaginal mucosa. Prognosis bad.	Vaginal hysterectomy. Bougie in ureter. Pus cavity beside uterus in abdomen.	3-5-94	Five months after operation.	Local return. Death sudden.
M. E.	Cervix. Vagina and parametrium involved. Bad prognosis.	Vaginal hysterectomy. Nodule in broad lig. dissected out.	3-5-94	Eight months after operation.	Local return.
M. H.	Cervix.	Vaginal hysterectomy.	3-7-94	Died from operation.	Death due to peritonitis.
M. Q.	Cervix.	Vaginal hysterectomy.	8-21-94	Died from operation.	Death due to peritonitis.
B. Z.	Portio vaginalis. Disease had encroached upon vaginal walls 2 cm.	Vaginal hysterectomy. Ureter cut.	8-22-94		Ureter dissected out and sutured into incision in bladder. 8-15-95, no sign of return. No urinary difficulty.
M. P.	Body.	Abdominal hysterectomy.	7-25-94		Perfect health when last seen, 8-18-95.
A. R.	Cervix.	Combined operation, vaginal and abdominal.	8-8-94		No local induration or ulceration. Good health, 8-16-95.
S. A.	Cervix. Converted into shell.	Combined operation, vaginal and abdominal.	6-5-94		Doctor writes that patient is in good condition, with no sign of recurrence of disease, 10-16-95.
K. A.	Body.	Supra-vaginal amputation. Cervix cupped out.	6-20-94		No evidence of recurrence, 9-12-95.
S. C.	Cervix.	Vaginal hysterectomy. Tube caught in vaginal incision.	2-17-94		Patient in good health and without symptoms pointing to return, 9-17-95.
Mrs. W.	Cervix.	Vaginal hysterectomy.	11-15-91	Died about eighteen months after operation.	Carcinoma of breast removed about one year after the vaginal hysterectomy. Patient died of heart lesion.

NOTES ON SOME CASES OF ANGINA TREATED WITH BEHRING'S ANTITOXINE.

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The following cases of angina, either due to the bacillus diphtheriae, or simulating true diphtheria and due to other organisms, have been observed in the hospital since the introduction of the antitoxine treatment.

Some of the cases are of interest as relating to the effect of the antitoxine on diphtheria; others were not treated by antitoxine, but present some special point of interest bearing more or less upon diphtheritic or diphtheroid inflammations.

In the cases treated by antitoxine, the preparation prepared under the direction of Behring was exclusively used, the various strengths being indicated according to the severity of the case and regardless of the age of the patient.

The antitoxine was usually injected into the cellular tissue of the back, though occasionally into the musculature of the thigh, the injection being done with a syringe previously sterilized by boiling, the skin of the part to be injected having been prepared by the methods usual before operative procedures.

The cases, which number eighteen, may be grouped under the following heads:

Membranous Angina due to the Bacillus Diphtheriae.

Case 1.—Female, aged 11, white. Admitted to the hospital December 31, 1894, complaining of sore throat.

History.—The family history is negative. The patient had measles, whooping cough and typhoid fever as a young child.

The present illness began four nights ago, the patient waking up in the middle of the night with an attack of nausea, followed by vomiting and headache. The throat did not feel sore until the following night, and she then noticed pain on swallowing. At first the soreness was confined to one side, but later both sides became involved.

On admission the general condition was good. There was great swelling of both tonsils, the glands almost meeting in the median line. The inner surface of each tonsil was lined by a purulent membrane, which, on removal, left a bleeding surface.

January 1. The membrane has extended to the uvula and soft palate. There is slight glandular swelling on the left side.

January 2. The child looks rather pale and is dull and apathetic. Behring's Antitoxine No. 3 was injected into the subcutaneous tissue of the back.

January 3. The child is much brighter, states that she feels better, and voluntarily asks for food. The swelling of the tonsils has diminished, though the uvula is still covered by membrane. The tense oedema of the tonsils and adjacent parts observed yesterday has disappeared.

January 4. The membrane has almost disappeared.

The temperature on admission was 101.5° F., and ranged between this point and 103° F. up to the time of the inoculation, when it was 103° F. Following the inoculation it sank gradually; the morning following it was 100.5° F., but after this never passed above 100° F., the convalescence being uninterrupted.

The pulse was noted to be a little feeble the day on which the inoculation was made; the following morning it was much improved. About six days after the inoculation the patient began to have attacks of urticaria, coming and going over a period of a week. The eruption was not confined to the region of the original injection, but occurred in various parts of the body.

Bacteriological Examination.—Cover-slips from the throat did not show definite diphtheria bacilli.

Cultures after 24 hours showed almost a pure culture of the bacillus diphtheriae.

A guinea-pig inoculated with a 24-hour bouillon culture died 14 days later with characteristic lesions, diphtheria bacilli being obtained from the seat of inoculation.

Case 2.—Female, aged 35, white. Admitted to the hospital January 7, 1895, complaining of sore throat.

History.—Her father died of some disease of the liver, her mother of heart disease. No other diseases in the family.

As a child she had the usual exanthems. She had an attack of diphtheria at 9 and another at 29, the latter being a severe attack. She has had four attacks of tonsillitis in the last three years.

The present illness began with a feeling of malaise three days ago; the following day she had chilly feelings and pain in the limbs and back. The throat was not noted to be sore till yesterday.

On admission the general condition was good. There was a general reddening of the throat and a large patch of grayish-white membrane over the left tonsil, which was detached with difficulty and left a bleeding surface.

Behring's Antitoxine No. 1 was injected into the muscles of the back.

January 8. The membrane on the left tonsil remains the same. There is a small patch on the right tonsil which was not noticed yesterday.

January 10. The membrane has completely disappeared.

The temperature on admission was 100.5° F. At the time of the inoculation, two hours later, it was 101.5° F., and had risen two hours later to 102° F. The following morning it had fallen to 100° F., but rose again slightly, reaching 100.5° F. at 4 P. M.; from this time on it fell, reaching normal in four hours and never again rising above that point. The pulse was good at all times. No skin eruption was observed.

Bacteriological Examination.—Cover-slips from the throat showed typical diphtheria bacilli. Cultures on blood serum showed many colonies of the bacillus diphtheriae and a few of the streptococcus pyogenes.

An animal inoculated with a 24-hour bouillon culture failed to react either locally or constitutionally.

The organism isolated was certainly not the pseudo-diphtheria bacillus. It acidified litmus bouillon, and grown side by side with a culture of the pseudo-bacillus, could easily be distinguished. The patient was discharged seven days after the disappearance of the membrane, the bacilli still being present in the throat.

February 17. The patient again comes under observation after a five weeks' holiday. The throat is quite clear. She states that during her absence, and about three weeks after the cessation of the first attack, she had a second fairly severe attack of sore throat, which was diagnosed tonsillitis by the attending physician, but without a bacteriological examination.

Cultures were again from the throat, and diphtheria bacilli and streptococci found to be present.

The patient was kept under observation, and three days later cultures were again taken, the patient having used at frequent intervals for the preceding 24 hours a bichloride spray and a solution of hydrogen peroxide as a gargle. Large numbers of diphtheria bacilli were still present.

Two days later a third set of cultures were made, the patient in the meanwhile having had Löffler's toluol solution vigorously applied to both tonsils five or six times. The diphtheria bacilli were still present, though in smaller numbers.

These organisms, like those isolated in the first attack, were harmless for animals, so the patient was allowed to return to her work. Three weeks later she was again admitted to the ward with a history of having been taken with sore throat, fever and malaise four days previously. She had been attended

for a time by her own physician, and creosote had been applied locally. On admission there was a glossy white membrane over each tonsil, very tenacious in character. The patient was practically convalescent at this time. The membrane gradually disappeared and had entirely gone seven days from admission. There was no fever.

In the interval between the first and last attacks, and in the last attack, the diphtheria bacillus could always be obtained from the throat. It was on several occasions inoculated into animals and never produced either local or general reaction.

The organisms finally disappeared from the throat three days after the disappearance of the membrane caused by the last attack, or three months and three days from the beginning of the first attack.

Case 3.—Female, aged 8, white. Admitted to the hospital February 1, 1895, complaining of sore throat.

History.—The family history is negative. She has had the usual exanthems and has been treated for some chronic throat disease since August last.

The present illness began five days ago with a shaking chill lasting about half an hour. She felt well the next day until evening, when she had some fever. She complained of sore throat from the first.

On admission the general condition was good. The right tonsil was swollen and covered by a large patch of yellowish-gray membrane; the left tonsil also swollen and shows a smaller patch of membrane; the uvula free.

Behring's Antitoxine No. 2 was injected into the subcutaneous tissue of the back.

February 2. The membrane is still present, but looks swollen and has a shining translucent appearance.

February 3. The edges of the membrane are curling up. There is a fine pink papular eruption over the face and back, not itchy.

February 5. All the membrane has gone but a small patch over the right tonsil. The eruption has disappeared.

February 8. The child complains of itching of the back. There are ten to twelve urticarial wheals about the seat of inoculation.

February 9. The urticaria has disappeared.

The temperature on admission was 101° F., but had fallen to 99° F. when the inoculation was made; it never again passed 99.3° F. The pulse was always satisfactory.

Bacteriological Examination.—Cover-slips from the membrane showed a fair number of typical diphtheria bacilli. Cultures showed the same organism in an almost pure state.

A guinea-pig inoculated with a 24-hour bouillon culture died 76 hours later, the autopsy showing the typical lesions of experimental diphtheria, and the organism being recovered from the seat of inoculation.

The organism disappeared from the throat five days after the disappearance of the membrane.

Case 4.—Female, aged 30, white. Admitted to the hospital February 5, 1895, complaining of sore throat.

History.—The family history is unimportant. The patient had the usual exanthems as a child. She has had two attacks of appendicitis, the last one two years ago. She had right-sided pleurisy 20 months ago. Since the age of 15 she has had nine or ten attacks of tonsillitis, none of them very severe.

The present illness began two days ago with chilly feelings, which lasted for twenty-four hours. Last night she began to have frontal headache, which persisted up to a short time ago; all day yesterday she had pains through the limbs. The throat felt a little sore from the first.

On admission the general condition was good. The fauces and tonsils were slightly congested, the tonsils quite swollen, especially the right, which was almost covered with a patch of yellowish-gray adherent membrane; a smaller patch was present on the left tonsil.

Behring's Antitoxine No. 3 was injected into the subcutaneous tissue of the back. In the afternoon some pain at the seat of inoculation was complained of.

February 6. The patient feels much better. There is still some pain at the seat of inoculation. The throat is less swollen, though the patch on the left tonsil is somewhat increased in size.

February 7. The throat is almost clear; what membrane remains is swollen and pearly looking.

February 8. The membrane has entirely gone.

The temperature on admission at 2 P. M. was 102° F.; at 6 P. M., about two hours after the inoculation, it had risen to 102.5° F.; it then fell, reaching 99° F. at 8 the following morning. At 12 noon on the 6th the temperature was 100° F.; it then fell gradually, reaching normal at midnight and never again going higher than 99.6° F.

The pulse ranged from 76 to 106; it was always strong.

No skin eruption was noted.

Bacteriological Examination.—Cover-slips from the membrane showed typical diphtheria bacilli. Cultures showed the same organism associated with the staphylococcus aureus and a few streptococci.

A guinea-pig inoculated with a 24-hour bouillon culture showed marked local tumefaction, but did not die.

The diphtheria bacillus disappeared from the throat 22 days after the disappearance of the membrane.

Case 5.—Male, aged 26, white. Admitted to the hospital March 6, 1895, complaining of sore throat.

History.—Aside from a history of tuberculosis in two sisters the family history was negative. The patient had the usual exanthems as a child, and malaria and typhoid as an adult. He has been subject to attacks of sore throat ever since childhood, some of these attacks having been severe enough to confine him to bed.

The present illness began three days ago with dryness and, later on, soreness of the throat. No chill or fever. He has headache and pains through the limbs.

On admission the general condition was excellent. Both the tonsils were swollen and reddened, and the middle part of each was covered by a thick yellowish membrane, which, on being detached, did not cause bleeding. The neck glands were a trifle enlarged and tender.

Behring's Antitoxine No. 2 was injected into the subcutaneous tissue of the back.

The membrane gradually disappeared and was entirely gone three days after admission.

The temperature on admission was 99.5° F., and never again passed above 99° F. The pulse was always strong.

No skin eruption was noted.

Bacteriological Examination.—Cover-slips from the throat showed a few typical diphtheria bacilli. Cultures gave an almost pure growth of the same organism.

A guinea-pig inoculated with a 24-hour bouillon culture died 48 hours later, the autopsy showing typical lesions of experimental diphtheria, and the bacillus being recovered from the seat of inoculation

The organism disappeared from the throat three days after the disappearance of the membrane.

Case 6.—Male, aged 24, white. Admitted to the hospital March 10, 1895, complaining of sore throat.

History.—The family history is negative. The patient had the usual exanthems as a child, and la grippe and dengue as an adult. He has always been subject to attacks of tonsillitis.

The present illness began two days ago with soreness in the region of the left tonsil and chilly sensations. The attack began in the morning, and by evening a small patch of membrane was noticed on the left tonsil. On removing the membrane a bleeding surface was exposed.

On admission the general condition was good. The tonsils were swollen, and over each was a blackish eschar caused by the use of Löffler's toluol solution; beneath the eschar a gray membrane could be made out. The glands in the neck were slightly enlarged.

Behring's Antitoxine No. 3 was injected into the subcutaneous tissue of the back.

Two days after the inoculation the membrane had entirely disappeared, though the tonsils still looked a little red.

The temperature on admission was 104.8° F.; the next morn-

ing it had fallen to 99.5° F., and did not rise above 100.5° F. all that day. The following day it began to rise at 8 A. M., reaching 103.5° F. at noon, after which it fell gradually, being 99.5° F. at 8 the next morning and never again passing the normal. The pulse was always good.

No skin eruption was noted.

Bacteriological Examination.—Cover-slips from the throat showed a fair number of typical diphtheria bacilli. Cultures showed an almost pure growth of the same organism.

A guinea-pig inoculated with a 24-hour bouillon culture showed a marked local reaction, but did not die.

The bacilli were still present thirteen days after the membrane disappeared, though not virulent.

Case 7.—Male, aged 5, white. Admitted to the hospital June 13, 1895.

History.—Could not be obtained.

On admission it was noted that the child was small and ill-nourished. The skin was pale. The mucous membranes not cyanotic. The respiration was loud but not stridulous. There was a constant purulent discharge from the nostrils, and much muco-pus dribbled from the mouth. Membrane could be made out on the soft palate, but examination of the tonsils and pharynx was not satisfactory. The temperature was 105° F. on admission.

Behring's Antitoxine No. 2 was injected into the muscles of the right thigh. The child was practically moribund on admission and died suddenly eight hours later.

Bacteriological Examination.—Cover-slips showed the diphtheria bacillus and cocci in groups or chains. From the cultures the diphtheria bacillus and the streptococcus were isolated.

An autopsy was not permitted.

Case 8.—Female, aged 29 months, white. Admitted to the hospital with dyspnoea August 12, 1895.

History.—Family history negative. The patient had measles five weeks ago. She has had a discharge from the right ear for seventeen months.

The present illness began three days ago with cough. The child, however, ran about and played as usual up to last night. This morning about 4 A. M. she woke up with a severe attack of dyspnoea, which has gradually increased.

On admission the child was dull and apathetic. The mucous membranes and finger-tips were slightly cyanotic. There was marked obstruction to inspiration. Both tonsils were swollen and covered with a grayish exudate. There was no exudate on the posterior pharyngeal wall. Temperature 100.5° F.

Behring's Antitoxine No. 3 was injected into the subcutaneous tissue of the back.

The dyspnoea became rapidly worse about three hours after admission, and the patient died during an attempt at tracheotomy.

Bacteriological Examination.—Cover-slips from the membrane showed many typical diphtheria bacilli. Cultures showed the same organism. An autopsy was not permitted.

Case 9.—Male, aged 2 years and 10 months, white. Admitted September 8, 1895, complaining of sore throat.

History.—The family history was negative. The child has had no previous illness.

The present illness began five days before admission with anorexia. Two days later the child complained of pain on swallowing. This morning a membrane was discovered in his throat by his physician and he was brought to the hospital.

On admission the general condition was good. Both tonsils were swollen and covered with patches of grayish-yellow exudate extending on each side into the uvula. The pharynx is clean. The glands of the neck are not enlarged.

Behring's Antitoxine No. 2 was injected into the subcutaneous tissue of the back.

September 9. The membrane seems to have spread slightly. The child is bright.

September 10. The child is better; the membrane has ceased spreading.

September 11. The membrane has largely disappeared.

September 13. The throat is entirely clear.

The temperature on admission at 8 P. M. was 100.4° F. At 2 A. M., four hours after the inoculation, it reached 101.8° F.; it then fell gradually, reaching normal 24 hours later and never again passing 99.2° F. The pulse was always strong.

No skin eruption was noted.

Bacteriological Examination.—Cover-slips from the throat showed suggestive bacilli, but no typical ones. Streptococci were present in fair numbers. Cultures showed the diphtheria bacillus and the streptococcus.

A guinea-pig inoculated with a 24-hour bouillon culture of the bacillus died 48 hours later with the lesions of experimental diphtheria, the organism being recovered from the seat of inoculation.

Case 10.—Male, aged 2, white. Admitted to the hospital September 20, 1895, with difficulty in breathing.

History.—A satisfactory history cannot be obtained, as the mother speaks only Bohemian.

From the mother's account the child has only been ill twenty-four hours, its only symptoms being irritability and loss of appetite.

On admission the child looked ill. The breathing was rapid and slightly obstructed. The voice was, however, clear. Over the tonsils and the neighboring parts of the soft palate a thick white membrane was seen.

Behring's Antitoxine No. 2 was injected into the buttock.

The breathing was somewhat more obstructed in the evening and the voice a trifle brassy.

September 22. The membrane has entirely disappeared. The child looks perfectly well.

The temperature remained steadily up about 102° F. until the 23d, when it fell gradually, reaching 99.4° F. at 10 P. M. and not rising again.

Bacteriological Examination.—Cover-slips from the membrane showed a fair number of diphtheria bacilli. The cultures showed an almost pure culture of bacillus diphtheriae.

Case 11.—Male, aged 7, white. Admitted to the hospital November 4, 1895, complaining of sore throat.

History.—The family history is unimportant except that he lost one sister from croup. He has had measles but no other illness. The present illness began four days ago with pain in the throat, which was increased by swallowing. The pain was at its worst two days ago, and he felt weak at that time. The pain and the weakness are the only symptoms complained of.

On admission the general condition was good. Both tonsils were swollen and showed numerous areas of membrane formation with rather a patchy arrangement. There was also a patch of membrane on the soft palate to the right of the uvula. The breathing was somewhat harsh, but there was no great dyspnoea.

Behring's Antitoxine No. 2 was injected into the muscles of the left thigh.

November 6. The patient is quite comfortable; he has no pain on swallowing.

November 7. Only a small patch of membrane remains.

November 8. The membrane has quite gone.

The temperature on admission was 100° F., and sank following the inoculation to 98.8° F. It was up to 100° F. at noon on the 6th, and then fell gradually, never again reaching above 99.5° F.

Bacteriological Examination.—Cover-slips showed a good many typical diphtheria bacilli. Cultures showed the same organism, almost a pure growth.

The cases recorded in this group are of that class which from a clinical standpoint alone would be regarded as diphtheria, *i. e.* they are characterized by definite membrane formation. Aside from the question of the influence of the antitoxine on the progress of the disease they present no special points of interest, with the exception of Case 2.

This case is of interest from several points of view:

1. As showing the duration of antitoxine immunization and of natural immunization.

2. As showing the possibility of auto-infection.

3. As demonstrating that the diphtheria bacillus can exist for long periods in the throat.

4. As demonstrating the resistance of the diphtheria bacillus to chemical agents.

That the immunity conferred by the antitoxine (passive immunity) does not protect over as long a period as natural immunity (active immunity) has long been known as far as animals are concerned. Cases showing the duration of this artificial immunity in man are not, however, common. Henach has reported a case in which a recurrence of the disease occurred from 25 to 30 days after the use of the antitoxine, and Wolff-Lewin reports a case where a child who had apparently recovered perfectly after the use of antitoxine developed symptoms of a fresh attack ten days from the beginning of the first one. In our case the patient was immunized on January 7th and contracted a second attack of what was presumably diphtheria about three weeks later; it is true that the patient was not under observation during this second attack, but cultures made only a week later showed the diphtheria bacillus to be present in the throat. During this second attack no antitoxine was used, and yet a third attack occurred thirty-seven days after the beginning of the second. In this case, then, the period over which active immunity lasted would seem to be about thirty-seven days, whilst that over which passive (antitoxine) immunity lasted was only twenty-one days.

It seems highly probable that auto-infection occurs in most cases of croupous pneumonia and in many of streptococcus throat; it is also known that virulent diphtheria bacilli are occasionally found in the throats of healthy people. This case would seem to prove definitely that auto-infection does occur in diphtheria, as it was shown that the diphtheria bacilli were constantly present in the throat between the second and third attacks, the throat all this time presenting a perfectly normal appearance. It is only fair to conclude that when the immunity was worn out the individual became infected by the bacilli then present.

Although the patient was not under constant observation from January 7th, when the first attack began, until April 10th, when the diphtheria bacilli finally disappeared from the throat, yet cultures were made frequently enough to warrant the assumption that the bacilli were continuously present over the period between the dates specified. In an observation recorded in the British Medical Journal of which Sevestre speaks, the bacilli were obtained from the throat seven months after the disappearance of the membrane; but in this case the cultures were few and far between. The question of the survival of the diphtheria bacilli after the disappearance of the membrane is an important one from a prophylactic point of view, for we must admit the possibility if not the probability of individuals such as our patient transmitting the disease to others. Such a possibility once being established, the isolation of diphtheria cases would not be subject to any fixed law, but would depend on the demonstration of the presence or absence of the bacillus in the throat.

The fact that the bacilli in this case were only in part destroyed by the repeated action of Löffler's toluol solution is an interesting one, especially as the solution was acting on a throat devoid of membrane. The fact that the bacillus appears so resistant should not, however, deter us from the use of such chemical agents, as clinical experience has amply proved their value.

DIPHTHERIA SIMULATING FOLLICULAR TONSILLITIS.

Case 12.—Female, aged 23, white. Admitted to the hospital January 17, 1895, complaining of sore throat.

History.—The family history was unimportant. The patient had the usual exanthems as a child; she has not been subject to sore throat. The present illness began four days ago with backache, headache, sore throat and pains in the limbs. There was slight pain on swallowing.

On admission the general condition was good. Both the tonsils were swollen and on both sides covered with numerous yellowish patches, apparently plugging the follicles. No definite areas of membrane were to be made out.

Behring's Antitoxine No. 2 was injected into the subcutaneous tissue of the back.

January 18. This morning a small patch of membrane about the size of a split pea was noticed on the soft palate; it was quite adherent.

January 19. The membrane is disappearing.

January 21. The membrane has entirely gone.

The temperature on admission was 100.2° F., and about the same at the time the inoculation was made; the following morning it was 99° F., and never passed above this point subsequently. The pulse was always strong. There was some itching about the seat of inoculation three days after its performance, but no skin eruption was noticed.

Bacteriological Examination.—Cover-slips from the throat showed suspicious bacilli, but nothing definite. Cultures showed the diphtheria bacillus in practically pure culture.

A guinea-pig inoculated with a 24-hour bouillon culture showed marked local reaction, but did not die.

This case corresponds to those described by Koplik as acute lacunar diphtheria of the tonsils. It illustrates the necessity, not yet fully appreciated, of a bacteriological diagnosis in all cases of throat inflammation. It is just such cases as this which would be clinically regarded as a non-infectious tonsillitis, which may give rise to serious epidemics of diphtheria.

DIPHTHERIA WITHOUT MEMBRANE.

Case 13.—Female, aged 35, white. The patient has been in the hospital for fifteen months with progressive muscular atrophy. On February 17, 1895, she complained of sore throat. The throat was examined and found to be a little swollen and reddened, but there were no signs of membrane. On the 18th the throat was again examined and showed the same appearances. Cultures were made at this time and showed, the following day, many colonies of typical diphtheria bacilli.

The patient was transferred to the isolation ward January 19. Her throat then was a little swollen and reddened, but there were no signs of membrane. There was no dyspnœa, no running at the nose. The general condition was excellent. The throat remained reddened and swollen over a period of eight days, the swelling subsiding during this period and the redness decreasing.

The treatment consisted of a bichloride spray locally, and whiskey as a stimulant.

The temperature, which was 100.2° F. on the night of January 17, rose to 101.5° F. by noon of the next day, and remained up till 6 P. M.; it then gradually fell, reaching normal on the 19th and never passing 99.5° F. subsequently.

Bacteriological Examination.—Cover-slips did not show definite diphtheria bacilli. Cultures showed an almost pure growth of the bacillus diphtheriae.

A guinea-pig inoculated with a 24-hour bouillon culture showed a well-marked local reaction, but did not die.

This case again illustrates the necessity of a bacteriological diagnosis in all suspected throat cases; clinically, no feature was present in this case to indicate diphtheria.

Multiple Infection with Bacillus Diphtheriae.

Case 14.—Male, aged 4, white. Admitted to the hospital March 29, 1895, on account of fever and a discharge from the right ear.

History.—The family history is unimportant. The patient was in the hospital the June previous with malarial fever, but recovered completely. The present illness began three days ago with pain in the head. At this time the child was noticed to hold his hand constantly to the side of his head. The morning following the onset of the pain he seemed better, but it was noticed that there was a discharge from the right ear, which has continued since. His nose has been discharging for a month or two; he has never complained of sore throat.

March 31. On admission to the isolation ward the child looked rather pale and stupid. There was a thick, creamy, odorless discharge from the right ear which was very profuse. From both nostrils there was a thick muco-purulent discharge. There was no sign of membrane in the nose. The tonsils and pharynx were reddened, but showed no signs of membrane. The neck glands were enlarged, hard and tender to the touch. There was a small area of dullness at the base of the left lung over which the breathing was feeble. On the radial side of the right thumb there was an excoriated area at the root of the nail. This area was covered by a whitish-yellow membrane, which, on being stripped off, left a raw, non-bleeding surface.

Behring's Antitoxine No. 2 was injected into the subcutaneous tissue of the back.

April 2. The child seems about the same. The ear is still discharging profusely; the nose less so than formerly. A slight membrane has reformed over the wound in the right thumb. The throat is perfectly clear. In the afternoon the child did not look quite so well.

April 3. The child looks better this morning. About midday the left ear was noticed to be discharging; the patient had not complained of any pain in the ear region. There is still a slight membrane over the right thumb.

April 4. The left thumb is excoriated at its base; there is no membrane over the excoriation.

The child was taken home against advice this afternoon.

The temperature on admission to the hospital was 104° F. It sank in the evening to 101° F., and from March 30 to the time of admission to the isolating ward varied between normal and 101° F. At the time of the injection of the antitoxine the temperature was 100.8° F.; it sank gradually over the next forty-eight hours, the highest point reached after the inoculation being 101° F. at 8 P. M. on the day following. The pulse was always fairly strong.

No reaction about the seat of inoculation and no skin eruption was noted.

Bacteriological Examination.—Cover-slips from the discharge from the right ear showed the predominating organism to be a bacillus morphologically resembling the diphtheria bacillus; a good many cocci in chains were also present. Cultures showed many typical diphtheria bacilli and a fair number of streptococci.

A guinea-pig inoculated with a 24-hour bouillon culture showed very marked local reaction and was very ill for two or three days, but eventually recovered.

Cultures from the nasal cavity, the tonsils and the pharynx all showed the bacillus diphtheriae associated with the streptococcus pyogenes; in the tubes from the nasal cavity a few colonies of the staphylococcus aureus were also present.

Cultures from the right thumb showed the diphtheria bacillus with the streptococcus pyogenes and the staphylococcus aureus. Cultures from the left thumb showed the diphtheria bacillus and the streptococcus pyogenes.

The organisms were still present when the child was removed from the hospital.

The two main points of interest in this case are the double otitis media and the occurrence of wound diphtheria.

It is possible that many cases of otitis media in which the diphtheria bacillus is concerned are overlooked, the reported cases not being very numerous. Councilman has reported cases in this country, and Kossel and Kutscher in Germany. In Kossel's cases the diphtheria bacillus could not be isolated from the throat, though membrane was present, a fact which Kossel explains by the overgrowth of the diphtheria bacillus in this locality by other organisms. Most of these cases of otitis media have not been pure diphtheria infections, so that it is often impossible to say whether we are dealing with a primary mixed infection, or whether the diphtheria bacillus was the original causal factor and other organisms afterwards crept in.

Cases of wound diphtheria would also seem to be uncommon, that is if the term wound-diphtheria be limited to the infection of wounds with the Klebs-Löffler bacillus.

Abel has reported a case in which the diphtheria bacillus alone was present in the membrane, proving conclusively that this organism is capable of membrane formation *per se*, a fact which had been disputed by many writers.

It is interesting to note in our case, that while the diphtheria bacillus was obtained from the wound on each thumb, membrane was only present over the wound of the right thumb.

Angina Caused by the Pseudo-Diphtheria Bacillus.

Case 15.—Female, aged 22, white. The patient had been in the hospital for some weeks with chlorosis. On the evening of January 31, 1895, she complained of slight sore throat, and examination showed a reddened and swollen condition of the tonsils, with a small patch of membrane (?) on the left side. The next morning the membrane could not be seen and the patient felt perfectly well.

The temperature had risen sharply on the evening of the 31st to 100.5° F., but was normal by 8 A. M. the next morning, and no further elevation occurred.

Bacteriological Examination.—Cover-slips showed apparently characteristic diphtheria bacilli. The cultures were overlooked until the second morning after they were taken, when the medium was seen to be thickly studded with white colonies resembling diphtheria colonies. On cover-slips the organism much resembled the diphtheria bacillus; it was, however, shorter and thicker, and the individual organisms showed a strong tendency to lie in rows parallel to one another. Culturally, the organism also resembled the diphtheria bacillus, but was a much more profuse grower and alkalinized litmus milk.

A guinea-pig inoculated with a 24-hour bouillon culture showed neither local nor general reaction.

The organism could not be recovered from the throat eighteen days after the attack.

The organism isolated in this case corresponds in all its characteristics to that first described by Hofman and subsequently by Löffler and others. Koplik has described cases in which this organism was found, but not associated with membrane. The membrane in our case seems rather doubtful, as the examination at which the membrane was seen was made by candle light, and on the following morning no membrane was to be made out.

Membranous Angina simulating Diphtheria but due to Organisms other than the Klebs-Löffler Bacillus.

Case 16.—Male, aged 32, white. Admitted to the hospital January 24, 1895, complaining of sore throat.

History.—The family history was unimportant. The patient had the usual exanthems as a child and thinks he had diphtheria at three years of age.

The present illness began two days ago with severe headache and a violent shaking chill lasting about twenty minutes and followed by fever. The following day he felt better, but woke up on the morning of the third day with fever again. The throat has only been slightly sore.

On admission the general condition was good. Both tonsils were swollen and congested and covered with a thick gray-yellow membrane, which was quite densely attached. The uvula and soft palate were not invaded.

Behring's Antitoxine No. 3 was injected into the subcutaneous tissue of the back.

January 25. The patient feels much better. The membrane has partly disappeared.

January 26. The membrane has entirely disappeared.

The temperature on admission was 100° F.; it had risen to 102° F. two hours later, and then fell rapidly, reaching normal in twelve hours. The pulse was always strong.

Bacteriological Examination.—Cover-slips were negative for diphtheria bacilli.

In cultures the predominating organism was a short, slim bacillus which grew well on all media, producing a bright green pigment. The organism corresponded in all its culture reactions with the bacillus pyocyaneus.

Case 17.—Female, aged 41, white. The patient had been in the hospital for several months with acromegaly. She was admitted to the isolating ward January 25, 1895.

History.—The evening before admission the temperature rose and she complained of sore throat. The following morning, when the patient was seen, she was quite short of breath and sitting up in bed. Examination of the throat showed both tonsils to be much swollen and reddened. Over the left tonsil was a large grayish-yellow patch the size of a quarter, which had the appearance of false membrane. By 7.30 in the evening several spots of exudate were seen on both tonsils and the case presented more the appearance seen in follicular tonsillitis.

Behring's Antitoxine No. 3 was injected into the subcutaneous tissue of the back.

January 26. The throat looks a little better. The patches still remain, but the swelling has subsided somewhat.

January 27. The patches are fewer in number.

January 28. The exudate has almost gone. The patient complains of a little pain and stiffness in the neck and back.

The temperature on admission was 102° F. By the following morning it had fallen to 100° F., but rose again in the evening to 102° F. A similar exacerbation occurred the following day, after which the temperature gradually fell to normal. The pulse was strong all through the course of the illness.

No skin eruption was noted.

Bacteriological Examination.—Cover-slips showed no diphtheria bacilli; a variety of organisms were present, no one apparently predominating.

Cultures showed an almost pure culture of the streptococcus pyogenes.

Case 18.—Male, aged 31, white. Admitted to the hospital March 11, 1895, complaining of sore throat.

History.—The family history was unimportant. The patient had the usual exanthems as a child; he has not been subject to sore throats.

The present illness began three days ago with soreness of one, and later, of both sides of the throat. He had headache and general aching all over. No chill or chilly sensations.

On admission the general condition was good. The throat was congested, and the tonsils were much swollen, almost meeting in the middle line. On the inner side of each tonsil there was a sloughy-looking yellow-gray membrane. The neck glands were enlarged and tender.

Behring's Antitoxine No. 2 was injected into the subcutaneous tissue of the back.

In the evening of the day of admission the throat was so swollen that the patient had difficulty in swallowing even liquids.

March 12. The swelling is decreasing; the patient feels better.

March 14. The swelling is much less.

March 19. The membrane has entirely disappeared.

The temperature on admission was 103.5° F.; by 8 A. M. the next morning it was down to 101° F., but by 8 P. M. was up to 104° F.; it fell in the night, but rose the next afternoon to 102.5° F., after which it gradually sank to normal.

No skin eruption was noted.

Bacteriological Examination.—Cover-slips from the membrane showed numerous cocci in chains, but no diphtheria bacilli.

Cultures gave a practically pure growth of streptococcus pyogenes.

These cases again show the necessity of bacteriological examination in all inflammatory throat affections.

Case 16 is interesting from a bacteriological point of view, for, so far as we have been able to make out, a membranous angina due to the bacillus pyocyaneus has not been described hitherto. This organism, though usually comparatively harmless, has been described as a factor in various diseased conditions, usually in association with other organs; in our case it was apparently in pure culture, but this may be due to the fact that it had overgrown the organisms with which it was associated. The comparatively frequent presence of the pyocyaneus in chronic otitis media would lead one to suspect that it may not be an infrequent inhabitant of the nasal or buccal cavities.

THE EFFECT OF THE ANTITOXINE TREATMENT.

Of the eighteen cases above recorded, sixteen received the antitoxine treatment, three of these cases being non-diphtheritic.

While this of course is too small a number of cases on which to base any statistical conclusions, several facts in connection with the treatment seem worthy of attention.

Two of the cases died, but both of these were moribund on admission, one dying three and the other eight hours after admission, so that the antitoxine was given no chance.

The other thirteen diphtheria cases were most of them mild, in fact none were very severe, but both on the general condition and on the temperature the antitoxine seemed to have a marked effect. It was almost invariably noticed that the day following the injection the patient was much brighter, and in the case of children the return of the appetite was the most marked indication of improvement.

In looking over the cases it will be noted that in those due to the bacillus diphtheriae the antitoxine, as a rule, caused a reduction of the temperature to the normal inside of twenty-four hours; in one or two of the cases there was a slight rise in the temperature eighteen to twenty hours after the inoculation, but in only one case was no effect on the temperature noted. The last two cases afford excellent examples of the effect of the antitoxine on non-diphtheritic cases; both were early cases, so that a spontaneous fall of temperature can be excluded, and in both the temperature was not influenced in the slightest degree by the antitoxine.

Skin eruptions following the antitoxine injections were noted in several of our cases; they have been noted by various observers since the inauguration of the treatment, but not enough stress has been laid on the fact that these eruptions are in all probability due to the serum *per se*, and not to the antitoxic agents contained therein. The deleterious effects of the serum of one species of animal when injected into a

member of another species are too well known to be repeated here, but it is interesting to know that Sevestre, by injecting horse-serum in twenty-centimetre doses into children with non-diphtheritic sore throats, was able to produce urticaria and other forms of skin eruption similar to those observed after the use of the antitoxine.

The skin eruptions were the only bad effects, if one could so call them, which were observed after the use of the antitoxine. No other appreciable symptoms plainly due to the injection could be observed, nor did the examination of the urine give evidence of any such.

PROCEEDINGS OF SOCIETIES.

THE JOHNS HOPKINS HOSPITAL MEDICAL SOCIETY.

Meeting of October 7, 1895.

Pyarthrosis—Discussion on Dr. Finney's paper. (See September-October BULLETIN, page 144.)

DR. HALSTED.—In these cases of knee-joint irrigation we do not hope to do more than to greatly inhibit the activity of the micro-organisms—to assist the tissues to destroy the micro-organisms. It is rarely necessary to do more than incise an acute abscess; the tissues do the rest. And yet we know that the tissues about the abscess have been invaded by the pyogenic micro-organisms. In irrigation of the knee-joint we do not expect to reach the micro-organisms outside of the joint.

In the last case reported by Dr. Finney—the one with triple infection—I do not feel at all sure that we could not have taken care of the joint itself. We amputated because in a few days we found the tissues in the thigh almost up to the hip-joint invaded by the organisms to a shocking extent, with lesions characteristic of the air-producing bacillus.

That solutions of bichloride of mercury are more efficacious than salt solutions in destroying and inhibiting pyogenic organisms outside of the body we have sufficient proof. There is also abundant clinical, if not wholly conclusive experimental evidence that the same is true in the tissue spaces, in joints, etc.

The irrigation of the urethra in the treatment of gonorrhœa furnishes a good clinical example of the benefits to be derived from solutions of corros. sub. Here, too, the specific micro-organisms have been demonstrated in the tissues outside of the urethra.

I speak from a great deal of experience, from daily observations for five years in the Roosevelt Hospital Dispensary, New York. In this work I was very ably assisted by Drs. Richard Hall and Frank Hartley of New York. The salt solutions are worse than ineffectual in the treatment of gonorrhœa. With them we never succeeded in aborting a case of gonorrhœa, either in private or dispensary practice, but we constantly induced a cystitis and epididymitis. With the bichloride irrigation, not a single case of cystitis or epididymitis occurred in these five years. I think that we have had the same experience in the dispensary here. Doctor Brown told me less than a year ago that he had never produced cystitis or epididymitis with bichloride irrigation. In private practice it is very common, indeed it is the rule, to abort a gonorrhœa within a week or ten days with bichloride irrigation. Previous to the use of this irrigation I used to dread to have a case of gonorrhœa come to my office; after its introduction I was glad to see them. The treatment became so popular that certain specialists in New York said that they would never use it because it was ruining their practice. Men after a few visits were cured. Nor would they return when a fresh urethritis was contracted. Furthermore, they taught their friends how to treat themselves. It would be too much of a digression to give the details of this treatment at this time. But I must ask your permission to say that everything depends upon the intelligent use of the method. The strength of the solution is determined by the use of the microscope and by the tolerance of the particular urethra. The strength to be used varies from 1–200,000 to 1–25,000. A tolerance of the stronger solutions has, usually, to be acquired. Men with red hair have, as a rule, sensitive urethræ.

The gonococci disappear promptly from the urethral discharge after irrigation with solutions of corrosive sublimate, but are uninfluenced, apparently, by irrigation with the salt solution.

A Case of Congenital Ptosis.—DR. THOMAS.

The patient, B. L., dispensary No. B 587, whom I wish to show to you to-night, is a boy fourteen years old. He applied at the dispensary a few days ago complaining that he was unable to open his left eye. No similar case had ever occurred in the family so far as was known. The patient was the eighth child and the only son. His birth was natural but difficult. It was noticed soon after birth that he did not open his left eye, and this condition has remained unchanged ever since. In other respects the boy has developed normally.

In looking at him you notice that while his right eye is widely opened, his left eye is nearly closed by the drooping upper lid. The skin of the forehead on the left side is drawn into deep furrows, as if he were trying to lift the eyelid by a strong action of the occipito-frontalis muscle. If the left eye be covered by the hand the forehead becomes smooth. When asked to look up, the patient opens his right eye wider, rolls the eyeball upward and contracts the occipito-frontalis on that side. On the left side the eyeball remains stationary, and the only noticeable change is a still greater contraction of the occipito-frontalis muscle; if, however, the left eye be passively opened, the eyeball is moved upward to some extent, but not so far as on the right side. In looking down, the eyes move normally, but the left upper lid does not follow the movement as does the right.

The lateral movements of the eyes are normal in extent, but there is a curious disassociation; they appear to move independently of each other. His pupils are equal, moderately

contracted; they react to light and during accommodation. Ophthalmoscopic examination shows the fundus to be normal. The facial muscles and those of mastication act normally.

In this case we have a congenital defect, consisting of a paralysis of the left levator palpebræ superioris, paresis of the superior rectus, and an associated over-action of the occipito-frontalis on the same side, forming the common picture of congenital ptosis. The disassociation of the ocular movements is also of interest.

Congenital ptosis is, in our experience, not a common affection, this being the first case which I have had an opportunity of studying. The cause of the trouble is believed to be some abnormality in the nucleus of the third nerve, from which the muscles involved receive their motor nerve fibres. As far as I know, but a single careful anatomical examination of such a case has been made. I refer to the case of Prof. Siemerling, reported in the *Archiv f. Psych. u. Nervenkrank.*, Vol. XXIII, p. 764, 1892. The patient died from general paralysis, but during life he showed no ocular symptoms referable to that disease except the Argyle-Robertson pupils. The congenital ptosis was of the left eye. Siemerling discovered a lesion in the dorsal and ventral parts of the principal group of cells in the nucleus of the third nerve, and what seemed remarkable, the lesion was bilateral, although the left upper lid was alone affected. The nucleus of the third nerve is a complicated structure. It is, however, impossible to go into this question to-night, as I want to call your attention to some other interesting points in connection with congenital ptosis.

In 1883 Mr. Marcus Gunn exhibited a case before the Ophthalmological Society of London, which showed remarkable associated movements of the paralysed eyelid. When the patient opened his mouth or moved his jaw towards the right, the paralysed left upper lid was raised. This case created a great deal of attention, and a committee including Dr. Gowers, Dr. Stephen McKenzie and others was appointed to examine the patient. They confirmed Mr. Gunn's observation and expressed the opinion that in that case the levator palpebræ "is innervated both from the nucleus of the third nerve and from the external pterygoid portion of the nucleus of the fifth nerve."

Since the publication of this case, a number of cases have been reported, and in May, 1894, Bernhardt (*Neurol. Centralblt.*, Vol. XIII, p. 325) was able to collect twenty-four cases, eighteen of which he used for comparison. In nearly all of these the associated movement of the paralyzed lid occurred, either when the mouth was opened or the jaw moved away from the side on which the ptosis was present, *i. e.* during the action of muscles supplied by the fifth nerve. In two remarkable cases the fallen lid was raised when the other eye was voluntarily closed, an associated movement between a muscle supplied by the facial nerve on one side and one supplied by the third nerve of the opposite side.

The extent of the associated movement apparently varies in the different cases. The most striking report that I have seen was published in the *Archives of Ophthalmology*, Vol. XXII, p. 65, 1893, by Dr. A. A. Hubbell, in which there are three excellent photographs, illustrating this associated movement. In this case the paralyzed upper lid was raised quite as much if not more than the normal one when the mouth was opened.

As you see, when the patient whom I have here to-night opens his mouth wide, or moves the lower jaw strongly towards the right, there is no very evident raising of the left upper lid. If, however, careful measurements are made, it is found that the visual aperture widens two or three mm. The widening is greater when the patient looks down during the movement of the jaws. Voluntary closure of the right eye produces no effect on the left. It is not at all certain that this slight widening of the aperture is due to a contracture of the levator palpebrae and not to other mechanical causes.

The explanation of these associated movements is not clear. Most observers agree with the English committee in the belief that it is due to the third nerve's receiving axis cylinder processes from cells situated in the fifth nucleus. We know that fibres running in motor nerves may arise from cells quite widely separated in the central nervous system. You will see from the diagrams of the nuclei of the motor cranial nerves, which I have placed on the blackboard, the relative positions of the third and fifth nuclei. The third nucleus is under the aqueduct of Sylvius; the principal motor nucleus of the fifth is about the middle of the upper half of the fourth ventricle. The descending root of the fifth extends quite to the level of the third nucleus. There is some doubt as to whether this root should be considered sensory or motor. It is not difficult to believe that nerve cells might send their axis cylinder processes from either the motor nucleus, or from the nucleus from which the descending root arises, to leave the brain by the third nerve. If such a condition underlies the associated movements which occur in congenital ptosis, the question suggests itself whether the condition is a normal one, or whether it only occurs in connection with the abnormality of the third nucleus upon which the ptosis depends. In two cases in which the ptosis was acquired as one of the symptoms of ophthalmoplegia externa due to nuclear disease, Dr. Hughlings Jackson was unable to demonstrate any associated movements of the paralysed lids, and in the case before you I have not been able to convince either you or myself that there is any actual contraction of the paralysed levator muscle. These cases, so far as they go, would seem to indicate that this connection is not always present. I know of no anatomical investigations that bear on the subject.

Dr. Jackson, in the article referred to above (*Lancet*, Jan. 6, 1894), suggests another interesting question in connection with cases of congenital ptosis, *i. e.* whether Müller's muscle is also paralysed. You may remember that the eyelid contains, besides the levator palpebræ, smooth muscular fibres, the so-called Müller's muscle, which help to elevate the lid. This muscle receives its nervous supply from the cervical sympathetic. These nerve fibres leave the spinal cord by the upper four or five dorsal roots. The nerve cells from which they arise have not been localized, but it is believed that they are situated somewhere near the third nucleus. Since we believe that congenital ptosis is due to some central lesion, it is important to know whether Müller's muscle is paralysed. Dr. Jackson suggests a method by which this may be determined. It was pointed out by Jessop (*Proceed. of Royal Soc.*,

Vol. XXXVIII, p. 432, 1885) that if a solution of cocaine be dropped into the eye the pupil dilates and the visual aperture widens. He demonstrated by experiments that this was due to a stimulation of the endings of the sympathetic nerve, causing contraction of the dilator muscles of the iris and of Müller's muscle in the lid. Dr. Jackson urges the importance of applying this test in nervous diseases wherever the sympathetic may be involved, and points out the desirability of testing a case of congenital ptosis in this manner.

We dropped into both eyes of this patient three or four drops of a four per cent. solution of cocaine. At the end of half an hour both pupils were dilated and the visual apertures of both eyes had widened about two mm. It would appear from this that the cocaine acted equally on the two sides and gave no evidence of paralysis of Müller's muscle.

Note.—The patient has been examined on several occasions since he was shown to the Society. The observations differ but little from those recorded, but it may be of interest to give the last note of the examination under cocaine.

December 9, 1895. 10.50 a. m., visual aperture, R. eye opened normal, 12.5 mm.

L. eye opened normally, 5 mm. Eye wide open, 5 mm. Pupils equal, about 5 mm. in diameter. One minim of an 8-per cent. solution of cocaine was put into each eye.

11.40 a. m., visual aperture. R. eye opened normally, 11 mm. Wide open, 15 mm.

L. eye opened normally, 7.5 mm. Eye wide open, 8 mm., and with mouth open, 9 mm. Pupils equal, diameters about 9 mm.—H. M. T.

Dr. L. F. Barker.—The case which Dr. Thomas has shown is of more than ordinary interest. As to the connections of the nervus trigeminus and its motor and sensory nuclei with the nucleus nervi oculomotorii, there is little that can be said to have been definitely established. This much is certain, that fibres run from the gray matter connected with the sensory portion of the fifth nerve (*i. e.* the substantia gelatinosa near the spinal tract of the 5th and the so-called sensory nucleus of the 5th) into the fasciculus longitudinalis medialis, and the intimate relations of the latter bundle to the oculomotorius nuclei have been very definitely proven. Whether or not the motor nuclei of the trigeminus (nucleus princeps and nuclei minores [radicis descendentis]) are directly connected with the nuceus n. oculomotorii, does not as yet seem clear. A large amount of work has been done with regard to the various groups of ganglion cells of which the nucleus of the oculomotorius nerve is made up, but up to the present the cells which have to do with individual muscles have not been satisfactorily localized. Neurologists have recently been inspired with new hope as regards this point through the introduction of a new method of investigation. In June of last year Nissl of Frankfurt-am-Main, in an address in Baden-Baden (*Centralblt. für Nervenheilk. u. Psychiatrie*, 1894, Bd. XVII, pp. 337–344), described a procedure which, although of relatively narrow application, has the advantage of establishing exactly the location and relations of many of the nerve cells in the gray masses. For example, he states that the method will determine for each individual eye-muscle the localization of its corresponding nerve cells in the central nuclei, a result to which the most careful investigators with the use of other methods (*e. g.* v. Gudden's or Marchi's) have hitherto been unable to attain.

In an adult or half-grown animal a solution of continuity of the fibre connecting a nerve cell with a peripheral part, be it muscle fibre or epithelial surface, leads to retrogressive changes in the body of the nerve cell. These alterations, though somewhat different in nerve cells of different types, are very characteristic and easily recognizable, Nissl claims, after some experience. Very soon, too, changes occur in the neuroglia cells which are in the neighborhood of the affected neurons. The changes in the cells are recognizable in alcohol tissues sectioned and stained according to the latest directions of Nissl, and his staining reaction has to be looked upon as one of the most delicate we possess for the study of degenerations of the body of the nerve cell. In order to apply the method to the eye muscles, one would either extirpate a given muscle or cut the nerve supplying it, and subsequently (the lesions in the rabbit are most characteristic between the 8th and the 15th day) kill the animal and study serial sections of the nucleus of the third nerve. As Nissl points out, the very delicacy of the reaction necessitates the greatest caution in its application. Operations must be done aseptically, one must be absolute master of the technique and must be familiar with the appearances of the various cell-forms in the normal condition, otherwise the investigator will be led into serious error. Nissl suggests that his method be called "Die Methode der primären Reizung." Should this method prove to be as useful as it promises, and already confirmatory work has been done by other investigators, we can hope for a speedy settlement of the much vexed questions regarding the cells of the eye-muscle nuclei. Now that the importance of the gray matter in the anterior corpora quadrigemina as a governing centre for the various movements of the eye muscles is generally recognized, and the connections of the axons of the cells situated there by means of collaterals with the various eye-muscle nuclei have been definitely established, the possibility of an exact localization of the cells in the nuclei concerned directly with the individual muscles comes opportunely.

Another point in connection with the case Dr. Thomas has just reported seems to me worthy of remark.

In the formation of an associated movement there has been a marked dissociation of muscular contractions ordinarily associated. Dr. Thomas has spoken of the dissociation of movements of the muscles of the two eyes. Usually in contracting the frontalis muscle the fibres on both sides of the forehead are contracted at once. This boy possesses in an extraordinary degree the power of unilateral contraction of the frontalis; indeed, when his eyes are open the left frontalis is continually forcibly contracted, while the muscle on the right side is at rest. This is by no means surprising, for we know of many so-called associated movements which, through training and education, can be dissociated, as for example the isolation of finger movements observable in an accomplished pianist.

NOTES ON NEW BOOKS.

I. Vital Statistics of the District of Columbia and Baltimore, covering a period of six years ending May 31, 1890. By JOHN S. BILLINGS, M. D., Expert Special Agent. (*Washington, D. C.: Government Printing Office*, 1893.)

II. Vital Statistics of New York City and Brooklyn, covering a period of six years ending May 31, 1890. By JOHN S. BILLINGS, M. D., Surgeon U. S. A., Expert Special Agent. (*Washington, D. C.: Government Printing Office*, 1894.)

III. Vital Statistics of Boston and Philadelphia, covering a period of six years ending May 31, 1890. By JOHN S. BILLINGS, M. D., Surgeon U. S. A., Expert Special Agent. (*Washington, D. C.: Government Printing Office*, 1895.)

One hardly knows which to commend most, the patience with which the difficult and complicated results have been obtained by comparing and arranging the statistics in the above special volumes of the Eleventh Census, or the masterly manner in which the facts thus obtained have been arranged to elucidate many of the difficult problems of vital statistics. In these three volumes the comparative vital statistics of six important cities lying along the Atlantic coast have been presented; New York being compared with Brooklyn; Boston with Philadelphia, and Washington with Baltimore. The appropriateness of the comparison of New York with Brooklyn and Baltimore with Washington is obvious, as these cities are subject to the same climatic conditions and environment. The association of Philadelphia and Boston does not seem as natural, although it is possible that the dissimilarity of these cities in climate, location and character of population may be useful in giving emphasis to certain facts which are brought out more clearly by these differences. We learn that differences in death-rates are due to a variety of causes, such as race, sex, age, occupation, influence of poverty, ignorance of the laws of health on the part of the poor, abundance and cheapness of food-supply, dampness, pollution of soil, water-supply, house drainage and sewerage. Baltimore is an unsewered city, while Washington possesses a good system of sewers, and the latter, although more densely populated, has a lower death-rate than the former. In both cities the excessive death-rate of the colored race is explained by a high death-rate among children under five years of age. In both cities the highest death-rate is in low-lying districts near the harbors where there is the highest level of sub-soil water. In both cities the birth-rate among the colored people had decreased, and the proportion of deaths had decreased during the six-year period. The influence of a high level of sub-soil water is strikingly shown in New York by means of a transparent map of the original island of Manhattan with its marshes and water-courses, which can be placed over the colored maps showing deaths by sanitary districts during the six-year period under consideration, and which shows a greater mortality in the filled portions of the city. The same increased death-rate among dwellers upon filled ground is not shown in Boston, presumably because the back bay was filled with washed gravel, a much better material for underlying dwellings, and further because the made-land was occupied by the dwellings of the wealthy, who could live without crowding under excellent hygienic conditions.

The death-rate of New York is shown to be higher than that of any other city in the country, owing to the crowded condition of the island, the insanitary condition of the tenement houses, and the high infant mortality, especially among the children of foreigners. In this city the death-rate among children less than five years old is greatest among those children whose mothers had been born in Bohemia, and least among those whose mothers had been born in Poland and Russia, presumably of Jewish parentage, thus indicating the superior vitality of the Semitic stock. In Brooklyn, also, it was greatest among those whose mothers were born in Bohemia, but least among those whose mothers were born in Hungary, the latter evidently being a more resisting stock. In both Boston and Philadelphia deaths by consumption formed a very heavy percentage of the mortality. In Boston consumption claimed more victims than any other one form of disease; in Philadelphia but a single other disease, or rather combination of diseases, those of the nervous system, caused more deaths. There were more deaths from pneumonia in Boston than in Philadelphia, and the same was true of alcoholism. Typhoid fever, however, as might be supposed, when the water-supply of Philadelphia is considered, was a much more common cause of death in Philadelphia than in Boston.

It is interesting to notice that in all of these cities the determining influences which produce the greatest mortality from diarrhœal diseases are low-lying and tenement house districts, with an overcrowding of children. Diphtheria and croup are also especially fatal in low-lying water-side districts. It is true that these districts, in the absence of an epidemic of diphtheria and croup, may be free from any high mortality, but whenever an epidemic arises the death-rate is very high. It is impossible to do more than to glance briefly at a few of the many problems presented in these volumes. It is to be hoped that now their accomplished author has more leisure for work, by reason of his retirement from the U. S. Army Medical Corps, he may be induced to elaborate these into a monograph on the vital statistics of the great cities of the North Atlantic States. Whatever he may write will command wide attention from medical men and students of vital statistics, both in America and Europe.

A System of Surgery. Edited by FREDERIC S. DENNIS, M. D., assisted by JOHN S. BILLINGS, M. D. Vol. II. (*Philadelphia: Lea Bros. & Co.*, 1895.)

The second volume of this work can be as highly recommended as the first; we hope that the remaining volumes will be as good.

The book opens with a chapter on Minor Surgery and Bandaging, by Dr. Henry R. Wharton. The section on bandaging is excellently illustrated, mostly by means of photographic reproductions, and the directions for the application of bandages are clear and easily understood. The section on minor surgery is fairly complete, but a much more extensive account of the uses of massage in surgery would be in order, considering the important part it plays in the modern treatment of sprains and fractures.

Dr. Fowler's article on Plastic Surgery is well written. It deals with plastic surgery of the face and extremities only, however, no mention being made of the important plastic work in the genito-urinary tract in cases of epispadias, hypospadias, etc.

Dr. Forwood's article on Military Surgery deals principally with questions of transportation and field technique; it is clear and well written.

Dr. Senn's article on Diseases of the Bones is clear and concise; the sections dealing with the pathological anatomy are especially well worth reading.

Dr. Gibney's article on Orthopædic Surgery is an excellent one. We hope that his method of treating sprained ankle will become more generalized, now that a description of it has appeared in book form.

Dr. Stimson's article on Aneurism is complete, and contains many excellent illustrations.

Dr. Dennis' article on Diseases of the Vessels is very short, but is well written and illustrated.

Dr. Gerrish's article on Diseases of the Lymphatics contains two good plates, showing the distribution of the more important lymphatics and their relation to the neighboring glands, which should be very useful. The reading matter, especially the articles on filariasis and elephantiasis, is carefully done.

Dr. Roswell Park contributes a masterly article on Diseases and Injuries of the Head. The sections on Fracture of the Skull are especially clear and very complete.

Dr. Keen's article on the Surgery of the Spine, and Dr. Roberts' on Diseases of the Nerves are well up to the standard of the rest of the book.

Taken as a whole, the articles in this volume are well and carefully written, and as a rule contain numerous references which should be useful to those intending to go more deeply into the various subjects.

A Manual of the Modern Theory and Technique of Surgical Asepsis. Illustrated. By CARL BECK, M. D. (*Philadelphia: W. B. Saunders*, 1895.)

This little book is a valuable guide to surgeons who wish to refresh their memories as to the latest antiseptic technique. It is clearly written, abundantly illustrated, and is very helpful. It covers much the same ground as the little work of Dr. Robb reviewed in the BULLETIN a few months ago.

BOOKS RECEIVED.

The Principles and Practice of Medicine. Designed for the Use of Practitioners and Students of Medicine. By Wm. Osler, M. D. Second edition. 1895. 8vo. 1143 pages. D. Appleton & Co., New York.

Personal Reminiscences and Recollections of Forty-six Years' Membership in the Medical Society of the District of Columbia, and Residence in this City, with Biographical Sketches of Many of the Deceased Members. By Samuel C. Busey, M. D., LL. D. 1895. 8vo. 373 pages. Washington, D. C., 1895.

The Care of the Baby; A Manual for Mothers and Nurses, containing Practical Directions for the Management of Infancy and Childhood in Health and in Disease. By J. P. Crozer Griffith, M. D. 1895. 12mo. 392 pages. W. B. Saunders, Philadelphia.

Transactions of the Colorado State Medical Society. Twenty-fifth Annual Convention. By-Laws and List of Members. 1895. 8vo. 551 pages. Published for the Society. Denver, Col.

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INDEX TO VOLUME VI OF THE JOHNS HOPKINS HOSPITAL BULLETIN.

Abel, John J. Anæsthesia by ether (introductory note), 7;—Remarks on acute pancreatitis, disseminated fat necrosis and parapancreatitic abscess, 33;—Remarks on posture of the head in accidents under an anæsthetic, 5.

Abscess of liver perforating the lung, 144.

Acute pancreatitis, disseminated fat necrosis, parapancreatitic abscess, 32,

Amœbic dysentery, cases of, 142.

Anæsthesia by ether, 7.

Anthrax in a human being, 94.

Anthrax, literature on, 132.

Anthrax septicæmia in a human being, with acute anthrax endocarditis and peritonitis, 127.

Bacillus pyogenes filiformis (nov. spec.), 147.

Bacteriology and pathology of diphtheria, 39.

Barker, Lewellys F. Pharyngomycosis leptothrica, 93;—Remarks on case of congenital ptosis, 166.

Berkley, Henry J. Chorea minor occurring during an attack of maniacal excitement in an adult, 44;—Condition of the gemmules of the cortical neurodendron in insanity, 68;—Review of von Schrenck-Notzing's Therapeutic suggestion in psycopathia sexualis, 72.

Blumer, Geo. Notes on some cases of angina treated with Behring's antitoxine, 158.

Blumer, George, and Young, H. H. Anthrax septicæmia in a human being with acute anthrax endocarditis and peritonitis, 127.

Books received, 17, 36, 50, 95, 146, 168.

Brassfounder's ague, 48.

Brown, James. Catheterization of the male ureters, 12, 16.

Campbell, Given, and Ghiselin, A. D. Quick method of filtering blood serum, 91.

Carcinoma of the œsophagus, 32.

Cataract operations on the lower animals, literature of, 30.

Catheterization of the male ureters, 12, 16.

Chorea minor occurring during an attack of maniacal excitement in an adult, 44.

Clark, J. G. Death from chloroform, 89;—Radical method of hysterectomy for cancer of the uterus, 120.

Climatology and public health, 18.

Clinical and experimental study of the so-called oyster shucker's keratitis, 150.

Condition of the gemmules of the cortical neurodendron in insanity, 68.

Congenital amputation of forearm, 49.

Congenital hypertrophy of foot, 49.

Congenital ptosis, case of, 164.

Cullen, Thos. S. Rapid method of making frozen sections by the use of formalin, 67;—Tumor from aberrant adrenal in the kidney, 37.

Death from chloroform, 89.

De Schweinitz. The visual field as a factor in general diagnosis, 15.

Dreser, Prof. H. Anæsthesia by ether, 7.

Epispadias, 49.

Exhibition of cases, 32, 49.

Exhibition of specimens, 72.

Finney, J. M. T. Remarks on acute pancreatitis, disseminated fat necrosis, parapancreatitic abscess, 33;—Carcinoma of the œsophagus, 32;—Exhibition of surgical cases, 32;—Pyarthrosis, 144;—Schede's operation for varicose veins of the leg, 146; Specimen of stomach removed after Francke's operation for gastrostomy, 145;—Varicose veins, 32.

Fletcher, Robert. Medical lore in the older English dramatists and poets (exclusive of Shakespere), 73.

Flexner, Simon. Anthrax in a human being, 94;—Bacillus pyogenes filiformis (nov. spec.), 147;—Bacteriology and pathology of diphtheria, 39;—Exhibition of specimens, 72;—Peritonitis caused by micrococcus lanceolatus, 64;—Tuberculosis, cases of, 72.

Flexner, Simon, and Pease, H. D. Primary diphtheria of the lips and gums, 22.

Fracture of right femur, 49.
Futcher, T. B. Subcutaneous fibroid nodules, 133.
Ghiselin, A. D., and Campbell, G. Quick method of filtering blood serum, 91.
Gonorrhœal pyelitis and pyo-ureter cured by irrigation, 20.
Green hair, 48.
Halsted, W. S. Discussion of pyarthrosis, 164;—Remarks on the posture of the head in accidents under an anæsthetic, 4.
Hare, H. A. Posture of the head in accidents under an anæsthetic, 1–4.
Hyperpyrexia in typhoid fever, 143.
Ideal result following double tenotomy in a case of convergent strabismus, 70.
Johns Hopkins Medical Society, 15, 32, 45, 48, 69, 93, 142, 164.
Kelly, H. A. Gonorrhœal pyelitis and pyo-ureter cured by irrigation, 19;—Review of Busey's Personal reminiscences and recollections of forty-six years, 94;—Review of Robb's Technique, 35; Remarks on the posture of the head in accidents under an anæsthetic, 3;—Sigmoido-proctostomy, 30;—Uretero-cystostomy performed seven weeks after vaginal hysterectomy, 27.
McCormick, J. H. Psychologic development of medicine, 58.
McGee, Anita Newcomb. Review of Thornton's Dose book and manual of prescription writing, 50.
Medical lore in the older English dramatists and poets (exclusive of Shakespere), 73.
Myxœdema and exophthalmic goitre in sisters, 33.
New apparatus for applying plaster jackets, 25.
Notes on new books:—Beck's Manual of the modern theory and technique of surgical aseptics, 168;—Billings' Vital statistics of the District of Columbia and Baltimore, 167;—Billings' Vital statistics of New York City and Brooklyn, 167;—Billings' Vital statistics of Boston and Philadelphia, 167;—Burdett's Helps in sickness and to health, 146;—Busey's Reminiscences and recollections of forty-six years, 94;—Corrado Parona, 72;—Dennis and Billings' System of surgery, 125, 167;—Frothingham's Laboratory guide for the bacteriologist, 125;—Gleason's Essentials of the diseases of the ear, 50;—Gleason's Essentials of diseases of the nose and throat, 50;—Grandby's History of medicine and surgery in Georgia, 94;—Griffith's The care of the baby, 146;—Jackson's Essentials of refraction and the diseases of the eye, 50;—Purdy's Practical uranalysis and urinary diagnosis, 35;—Robb's Aseptic surgical technique with especial reference to gynecological operations, 35;—Sayre's Manual of organic materia medica and pharmacognosy, 36;—Tebaldi's Napoleone, una pagina storico-psicologica del genio, 16;—Thoma's Book of detachable diet lists, 125;—Thornton's Dose book and manual of prescription writing, 49;—Twenty-fifth annual report of the board of health of Massachusetts, 146;—Von Schrenk-Notzing's Therapeutic suggestion in psycopathia sexualis, 72;—Williams' Monograph on diseases of the breast, 16.
Notes on some cases of angina treated with Behring's antitoxine, 158.
Obituary:—James Brown, M. D., 95;—Arthur R. Oppenheimer, M. D., 95.
Oppenheimer, A. R. Brassfounder's ague, 48;—Green hair, 48;—Myxœdema and exophthalmic goitre in sisters, 33.
Osler, William. Abscess of liver perforating the lung, 144;—Hyperpyrexia in typhoid fever, 143;—Remarks on posture of the head in accidents under an anæsthetic, 4;—Remarks on progressive neural muscular atrophy, 48.
Pease, H. D., and Flexner, S. Primary diphtheria of the lips and gums, 22.
Peritonitis caused by micrococcus lanceolatus, 64.
Pharyngomycosis leptothrica, 93.
Platt, W. B. Congenital amputation of forearm, 49;—Congenital hypertrophy of foot, 49;—Epispadias, 49;—Fracture of femur, 49;—Undescended testicle, 49.
Posture of the head in accidents under an anæsthetic, 1.
Primary diphtheria of the mouth and gums, 22.
Proceedings of societies, 15, 32, 45, 69, 93, 142, 164.
Progressive neural muscular atrophy, 45.
Psychologic development of medicine, 58.
Pyarthrosis, 144, 164.
Quick method of filtering blood serum, 91.
Radical method of hysterectomy for cancer of the uterus, 120.
Randolph, Robert L. A clinical and experimental study of the so-called oyster shucker's keratitis, 150;—Two successful cataract operations on a dog, 28.
Rapid method of making frozen sections by the use of formalin, 67.
Robb, Hunter. Writings of Mauriceau, 51.
Russell, W. W. The clinical course of forty-seven cases of carcinoma of the uterus subsequent to hysterectomy, 154.
Schede's operation for varicose veins of the leg, 146.
Sigmoido-proctostomy, 30.
Specimens of stomach removed after Francke's operation for gastrostomy, 145.
Stiles, Wardell. Corrado Parona (review), 72.
Subcutaneous fibroid nodules, 133.
Subcutaneous fibroid nodules, literature of, 142.
Taylor, R. Tunstall. A new apparatus for applying plaster jackets, 25.
Tetany in pregnancy, 85.
Thayer, W. S. Acute pancreatitis, disseminated fat necrosis, parapancreatitic abscess, 32.
The clinical course of forty-seven cases of carcinoma of the uterus subsequent to hysterectomy, 154.
The visual field as a factor in general diagnosis, 15.
Theobald, S. Ideal results following double tenotomy in a case of convergent strabismus, 70.
Thomas, H. M. Case of congenital ptosis, 164;—Progressive neural muscular atrophy, 49;—Tetany in pregnancy, 85.
Treatment of diphtheria by antitoxine, 97.
Tuberculosis, cases of, 69.
Tumor from aberrant adrenal in the kidney, 37.
Two successful cataract operations on a dog, 28.
Undescended testicle, 49.
Uretero-cystostomy performed seven weeks after vaginal hysterectomy, 27.
Varicose veins, 32.
Visual field as a factor in general diagnosis, 15.
Welch, W. H. Remarks on pyarthrosis, 145;—Treatment of diphtheria by antitoxine, 97.
Wilson, Cunningham. Cases of amœbic dysentery, 142.
Writings of Mauriceau, 51.
Young, Hugh H., and Blumer, George. Anthrax septicæmia in a human being with acute anthrax endocarditis and peritonitis, 128.

ILLUSTRATIONS.

PAGE.
1. Inspiratory and expiratory movements in artificial respiration, Figs. I and II 2
2. Method of irrigation in pyelitis and pyo-ureter 20
3. Taylor's plaster jacket stool—position of patient when jacket is applied, Figs. 1 and 2 25
4. Method of uretero-cystostomy, Figs. 1, 2, 3, 4 27
5. Method of sigmoido-proctostomy, Figs. 1, 2, 3 31
6. Tumor of aberrant adrenal, Figs. 1, 2 39
7. Feet and hands in progressive neural muscular atrophy, Figs. 1, 2 46
8. Extra-uterine pregnancy (after Mauriceau), Figs. 1, 2, 3... 56
9. Apparatus for filtering blood serum, Figs. I, II, III 92
10. Anatomical relations of bladder, uterus, uterine artery and ureter, Fig. I 124
11. Uterus removed by vaginal hysterectomy, Figs. III, IV .. 124
12. Steps of operation and completed operation, Figs. II, V... 124

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